```
=> fil capl; d que nos 142; d que nos 147
FILE 'CAPLUS' ENTERED AT 17:09:29 ON 28 MAY 2004
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```

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```
FILE COVERS 1907 - 28 May 2004  VOL 140 ISS 23
FILE LAST UPDATED: 27 May 2004  (20040527/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE


L13             STR
L15          32 SEA FILE=REGISTRY SSS FUL L13
L19           1 SEA FILE=REGISTRY ABB=ON  PYRIDOXAL/CN
L20           1 SEA FILE=REGISTRY ABB=ON  PYRIDOXAMINE/CN
L21           1 SEA FILE=REGISTRY ABB=ON  54-47-7
L22          35 SEA FILE=REGISTRY ABB=ON  L15 OR (L19 OR L20 OR L21)
L23           1 SEA FILE=REGISTRY ABB=ON  ASPIRIN/CN
L24           1 SEA FILE=REGISTRY ABB=ON  HEPARIN/CN
L26           1 SEA FILE=REGISTRY ABB=ON  PPADS/CN
L27        7882 SEA FILE=CAPLUS ABB=ON  PLATELET AGGREGATION INHIBITORS+OLD,RTC
               S/CT
L28       14733 SEA FILE=CAPLUS ABB=ON  ANTICOAGULANTS/CW
L29        6623 SEA FILE=CAPLUS ABB=ON  L22
L30       40472 SEA FILE=CAPLUS ABB=ON  (L23 OR L24 OR L26)
L31        5220 SEA FILE=CAPLUS ABB=ON  HIRUDIN/OBI OR WARFARIN/OBI
L32           1 SEA FILE=REGISTRY ABB=ON  HEPARIN SODIUM/CN
L33        1109 SEA FILE=CAPLUS ABB=ON  L32
L34          28 SEA FILE=CAPLUS ABB=ON  ANTITHROMBOLYTIC?/OBI
L35        3007 SEA FILE=CAPLUS ABB=ON  THROMBOLYTIC?/OBI
L36       10128 SEA FILE=CAPLUS ABB=ON  ANTITHROMBO?/OBI
L37          69 SEA FILE=CAPLUS ABB=ON  L29 AND (L27 OR L28 OR L30 OR L31 OR
               (L33 OR L34 OR L35 OR L36))
L38        3257 SEA FILE=CAPLUS ABB=ON  CONCURRENT?/OBI
L39        3511 SEA FILE=CAPLUS ABB=ON  CODRUG#/OBI OR COADMIN?/OBI OR
               CONCOMITAN?/OBI
L40        2486 SEA FILE=CAPLUS ABB=ON  DRUG DELIVERY SYSTEMS+OLD/CT(L)COMB?/OB
               I
L41       31318 SEA FILE=CAPLUS ABB=ON  DRUG INTERACTIONS+OLD,NT/CT
L42           2 SEA FILE=CAPLUS ABB=ON  L37 AND (L38 OR L39 OR L40 OR L41)


L13             STR
L15          32 SEA FILE=REGISTRY SSS FUL L13
L19           1 SEA FILE=REGISTRY ABB=ON  PYRIDOXAL/CN
L20           1 SEA FILE=REGISTRY ABB=ON  PYRIDOXAMINE/CN
```

Searched by Barb O'Bryen, STIC 571-272-2518

```
L21            1 SEA FILE=REGISTRY ABB=ON  54-47-7
L22           35 SEA FILE=REGISTRY ABB=ON  L15 OR (L19 OR L20 OR L21)
L23            1 SEA FILE=REGISTRY ABB=ON  ASPIRIN/CN
L24            1 SEA FILE=REGISTRY ABB=ON  HEPARIN/CN
L26            1 SEA FILE=REGISTRY ABB=ON  PPADS/CN
L27         7882 SEA FILE=CAPLUS ABB=ON  PLATELET AGGREGATION INHIBITORS+OLD,RTC
               S/CT
L28        14733 SEA FILE=CAPLUS ABB=ON  ANTICOAGULANTS/CW
L29         6623 SEA FILE=CAPLUS ABB=ON  L22
L30        40472 SEA FILE=CAPLUS ABB=ON  (L23 OR L24 OR L26)
L31         5220 SEA FILE=CAPLUS ABB=ON  HIRUDIN/OBI OR WARFARIN/OBI
L32            1 SEA FILE=REGISTRY ABB=ON  HEPARIN SODIUM/CN
L33         1109 SEA FILE=CAPLUS ABB=ON  L32
L34           28 SEA FILE=CAPLUS ABB=ON  ANTITHROMBOLYTIC?/OBI
L35         3007 SEA FILE=CAPLUS ABB=ON  THROMBOLYTIC?/OBI
L36        10128 SEA FILE=CAPLUS ABB=ON  ANTITHROMBO?/OBI
L37           69 SEA FILE=CAPLUS ABB=ON  L29 AND (L27 OR L28 OR L30 OR L31 OR
               (L33 OR L34 OR L35 OR L36))
L45        15588 SEA FILE=CAPLUS ABB=ON  EMBOLI?/OBI OR THROMBOEMBOLI?/OBI OR
               THROMBOS!S/OBI
L46        14187 SEA FILE=CAPLUS ABB=ON  CLOT#/OBI
L47            2 SEA FILE=CAPLUS ABB=ON  L37 AND (L45 OR L46)


=> s l42 or l47

L113           4 L42 OR L47

=> fil uspatf; d que nos l65

FILE 'USPATFULL' ENTERED AT 17:09:30 ON 28 MAY 2004
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 27 May 2004 (20040527/PD)
FILE LAST UPDATED: 27 May 2004 (20040527/ED)
HIGHEST GRANTED PATENT NUMBER: US6742188
HIGHEST APPLICATION PUBLICATION NUMBER: US2004103464
CA INDEXING IS CURRENT THROUGH 27 May 2004 (20040527/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 27 May 2004 (20040527/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2004
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2004

>>>  USPAT2 is now available.  USPATFULL contains full text of the     <<<
>>>  original, i.e., the earliest published granted patents or         <<<
>>>  applications.  USPAT2 contains full text of the latest US         <<<
>>>  publications, starting in 2001, for the inventions covered in     <<<
>>>  USPATFULL.  A USPATFULL record contains not only the original     <<<
>>>  published document but also a list of any subsequent              <<<
>>>  publications.  The publication number, patent kind code, and      <<<
>>>  publication date for all the US publications for an invention     <<<
>>>  are displayed in the PI (Patent Information) field of USPATFULL   <<<
>>>  records and may be searched in standard search fields, e.g., /PN, <<<
>>>  /PK, etc.                                                         <<<

>>>  USPATFULL and USPAT2 can be accessed and searched together        <<<
>>>  through the new cluster USPATALL.  Type FILE USPATALL to          <<<
>>>  enter this cluster.                                               <<<
>>>                                                                    <<<
>>>  Use USPATALL when searching terms such as patent assignees,       <<<
>>>  classifications, or claims, that may potentially change from     <<<
>>>  the earliest to the latest publication.                           <<<
```

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L13              STR
L15           32 SEA FILE=REGISTRY SSS FUL L13
L19            1 SEA FILE=REGISTRY ABB=ON  PYRIDOXAL/CN
L20            1 SEA FILE=REGISTRY ABB=ON  PYRIDOXAMINE/CN
L21            1 SEA FILE=REGISTRY ABB=ON  54-47-7
L22           35 SEA FILE=REGISTRY ABB=ON  L15 OR (L19 OR L20 OR L21)
L23            1 SEA FILE=REGISTRY ABB=ON  ASPIRIN/CN
L24            1 SEA FILE=REGISTRY ABB=ON  HEPARIN/CN
L26            1 SEA FILE=REGISTRY ABB=ON  PPADS/CN
L32            1 SEA FILE=REGISTRY ABB=ON  HEPARIN SODIUM/CN
L49          273 SEA FILE=USPATFULL ABB=ON  L22
L50         3825 SEA FILE=USPATFULL ABB=ON  L26 OR L23 OR L24 OR L32
L51         3552 SEA FILE=USPATFULL ABB=ON  (ASPIRIN OR HEPARIN OR HIRUDIN OR
                 WARFARIN)/IT
L53         2486 SEA FILE=USPATFULL ABB=ON  (THROMBOLYTIC? OR ANTITHROMBO?)/IT
L54         4462 SEA FILE=USPATFULL ABB=ON  (EMBOLI? OR THROMBOEMBOLI? OR
                 THROMBOS!S )/IT,TI,AB,CLM
L56          930 SEA FILE=USPATFULL ABB=ON  ((REDUC? OR INHIBIT? OR PREVENT? OR
                 DECREAS?)(3A)CLOT?)/IT,TI,AB,CLM
L58        77928 SEA FILE=USPATFULL ABB=ON  (INTERACT? OR POTENTIAT? OR
                 SYNERG?)/IT,TI,AB,CLM
L59        41309 SEA FILE=USPATFULL ABB=ON  (CODRUG# OR COADMIN? OR CONCOMITAN?
                 OR CONCURRENT?)/IT,TI,AB,CLM
L62         2355 SEA FILE=USPATFULL ABB=ON  L58(5A)DRUG#/IT,TI,AB,CLM
L65            8 SEA FILE=USPATFULL ABB=ON  L49 AND ((L50 OR L51) OR L53) AND
                 (L54 OR L56 OR L62 OR L59)
```

=> fil toxcenter; d que nos l74

FILE 'TOXCENTER' ENTERED AT 17:09:31 ON 28 MAY 2004
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FILE COVERS 1907 TO 25 May 2004 (20040525/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

TOXCENTER has been enhanced with new files segments and search fields.
See HELP CONTENT for more information.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a description of changes.

```
L13              STR
L15           32 SEA FILE=REGISTRY SSS FUL L13
L19            1 SEA FILE=REGISTRY ABB=ON  PYRIDOXAL/CN
L20            1 SEA FILE=REGISTRY ABB=ON  PYRIDOXAMINE/CN
L21            1 SEA FILE=REGISTRY ABB=ON  54-47-7
L22           35 SEA FILE=REGISTRY ABB=ON  L15 OR (L19 OR L20 OR L21)
L23            1 SEA FILE=REGISTRY ABB=ON  ASPIRIN/CN
L24            1 SEA FILE=REGISTRY ABB=ON  HEPARIN/CN
L26            1 SEA FILE=REGISTRY ABB=ON  PPADS/CN
L32            1 SEA FILE=REGISTRY ABB=ON  HEPARIN SODIUM/CN
```

```
L66          1735 SEA FILE=TOXCENTER ABB=ON  L22
L67         40155 SEA FILE=TOXCENTER ABB=ON  L26 OR L23 OR L24 OR L32
L68         56448 SEA FILE=TOXCENTER ABB=ON  (ASPIRIN OR HEPARIN OR HIRUDIN OR
                  WARFARIN)
L69          9351 SEA FILE=TOXCENTER ABB=ON  (THROMBOLYTIC? OR ANTITHROMBO?)
L70         33056 SEA FILE=TOXCENTER ABB=ON  (EMBOLI? OR THROMBOEMBOLI? OR
                  THROMBOS!S )
L71          1426 SEA FILE=TOXCENTER ABB=ON  ((REDUC? OR INHIBIT? OR PREVENT? OR
                  DECREAS?)(3A)CLOT?)
L72         85053 SEA FILE=TOXCENTER ABB=ON  (CODRUG# OR COADMIN? OR CONCOMITAN?
                  OR CONCURRENT?)
L74             3 SEA FILE=TOXCENTER ABB=ON  L66 AND (L67 OR L68) AND (L69 OR
                  L70 OR L71 OR L72)

=> fil embase; d que l87; d que l88

FILE 'EMBASE' ENTERED AT 17:09:32 ON 28 MAY 2004
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 FILE COVERS 1974 TO 28 May 2004 (20040528/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

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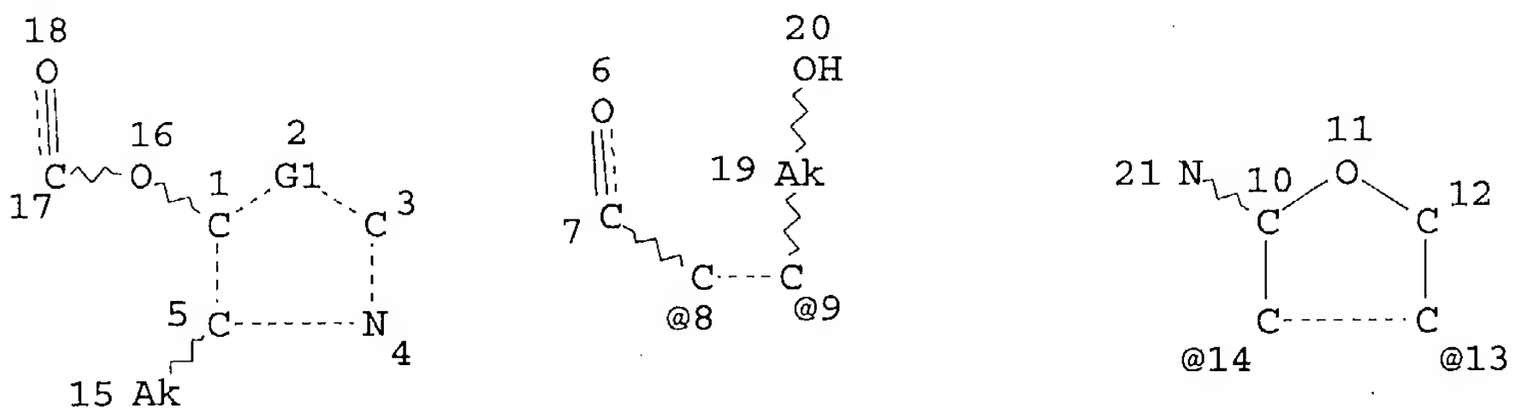
L13                 STR
```




```
VAR G1=8-1 9-3/14-1 13-3
NODE ATTRIBUTES:
NSPEC    IS RC      AT  21
CONNECT IS E1  RC AT  15
CONNECT IS E2  RC AT  19
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  21

STEREO ATTRIBUTES: NONE
L15            32 SEA FILE=REGISTRY SSS FUL L13
L19             1 SEA FILE=REGISTRY ABB=ON  PYRIDOXAL/CN
L20             1 SEA FILE=REGISTRY ABB=ON  PYRIDOXAMINE/CN
L21             1 SEA FILE=REGISTRY ABB=ON  54-47-7
L22            35 SEA FILE=REGISTRY ABB=ON  L15 OR (L19 OR L20 OR L21)
L26             1 SEA FILE=REGISTRY ABB=ON  PPADS/CN
L75          3238 SEA FILE=EMBASE ABB=ON  L22
L76          2968 SEA FILE=EMBASE ABB=ON  PYRIDOXAL 5 PHOSPHATE/CT OR PYRIDOXAMIN
                  E/CT
```

Searched by Barb O'Bryen, STIC 571-272-2518

```
L77          539 SEA FILE=EMBASE ABB=ON  PYRIDOXAL/CT
L78           27 SEA FILE=EMBASE ABB=ON  PYRIDOXAL DERIVATIVE/CT
L80       113869 SEA FILE=EMBASE ABB=ON  THROMBOEMBOLISM+NT/CT
L81         2368 SEA FILE=EMBASE ABB=ON  THROMBOSIS PREVENTION/CT
L82          379 SEA FILE=EMBASE ABB=ON  L26
L83          409 SEA FILE=EMBASE ABB=ON  "PYRIDOXAL PHOSPHATE 6 AZOPHENYL 2',4'
                 DISULFONIC ACID"/CT
L84        68165 SEA FILE=EMBASE ABB=ON  ACETYLSALICYLIC ACID/CT
L85        56380 SEA FILE=EMBASE ABB=ON  HEPARIN/CT
L86         6916 SEA FILE=EMBASE ABB=ON  ANTITHROMBOCYTIC AGENT/CT
L87            1 SEA FILE=EMBASE ABB=ON  (L75 OR L76 OR L77 OR L78) AND (L82 OR
                 L83 OR L84 OR L85 OR L86) AND (L80 OR L81)



L76         2968 SEA FILE=EMBASE ABB=ON  PYRIDOXAL 5 PHOSPHATE/CT OR PYRIDOXAMIN
                 E/CT
L77          539 SEA FILE=EMBASE ABB=ON  PYRIDOXAL/CT
L78           27 SEA FILE=EMBASE ABB=ON  PYRIDOXAL DERIVATIVE/CT
L83          409 SEA FILE=EMBASE ABB=ON  "PYRIDOXAL PHOSPHATE 6 AZOPHENYL 2',4'
                 DISULFONIC ACID"/CT
L84        68165 SEA FILE=EMBASE ABB=ON  ACETYLSALICYLIC ACID/CT
L85        56380 SEA FILE=EMBASE ABB=ON  HEPARIN/CT
L88            1 SEA FILE=EMBASE ABB=ON  (L76 OR L77 OR L78)(L)CB/CT AND (L83
                 OR L84 OR L85)(L)CB/CT
```

CB = drug combination

```
=> s l87 or l88

L114           2 L87 OR L88

=> fil medl; d que l101; d que l105

FILE 'MEDLINE' ENTERED AT 17:09:33 ON 28 MAY 2004

 FILE LAST UPDATED: 27 MAY 2004 (20040527/UP).  FILE COVERS 1951 TO DATE.

 On February 29, 2004, the 2004 MeSH terms were loaded.  See HELP RLOAD
 for details. OLDMEDLINE now back to 1951.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2004 vocabulary.  See http://www.nlm.nih.gov/mesh/ and
 http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a
 description of changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

L89         5207 SEA FILE=MEDLINE ABB=ON  PYRIDOXAL/CT OR PYRIDOXAL PHOSPHATE/CT

L90          373 SEA FILE=MEDLINE ABB=ON  PYRIDOXAMINE/CT
L93        12814 SEA FILE=MEDLINE ABB=ON  FIBRINOLYTIC AGENTS/CT
L94        11520 SEA FILE=MEDLINE ABB=ON  PLATELET AGGREGATION INHIBITORS/CT
L95        25257 SEA FILE=MEDLINE ABB=ON  ASPIRIN/CT
L96        35790 SEA FILE=MEDLINE ABB=ON  HEPARIN/CT
L97         1778 SEA FILE=MEDLINE ABB=ON  HIRUDIN/CT
L98         7694 SEA FILE=MEDLINE ABB=ON  WARFARIN/CT
L99       109810 SEA FILE=MEDLINE ABB=ON  "EMBOLISM AND THROMBOSIS"+NT/CT
L101           1 SEA FILE=MEDLINE ABB=ON  (L89 OR L90) AND (L93 OR L94 OR L95
                 OR L96 OR L97 OR L98) AND L99
```

Searched by Barb O'Bryen, STIC 571-272-2518

```
L89          5207 SEA FILE=MEDLINE ABB=ON  PYRIDOXAL/CT OR PYRIDOXAL PHOSPHATE/CT

L90           373 SEA FILE=MEDLINE ABB=ON  PYRIDOXAMINE/CT
L93         12814 SEA FILE=MEDLINE ABB=ON  FIBRINOLYTIC AGENTS/CT
L95         25257 SEA FILE=MEDLINE ABB=ON  ASPIRIN/CT
L96         35790 SEA FILE=MEDLINE ABB=ON  HEPARIN/CT
L97          1778 SEA FILE=MEDLINE ABB=ON  HIRUDIN/CT
L98          7694 SEA FILE=MEDLINE ABB=ON  WARFARIN/CT
L102        14833 SEA FILE=MEDLINE ABB=ON  PLATELET AGGREGATION/CT(L)(DE OR
                  PC)/CT
L103         2768 SEA FILE=MEDLINE ABB=ON  PLATELET ADHESIVENESS/CT(L)(DE OR
                  PC)/CT
L105            4 SEA FILE=MEDLINE ABB=ON  (L89 OR L90) AND (L93 OR (L95 OR L96
                  OR L97 OR L98)) AND (L102 OR L103)
```

DE = drug effects ~~effects~~

PC = prevention & control

```
=> s l101 or l105

L115            4 L101 OR L105

=> fil wpids; d que l112

FILE 'WPIDS' ENTERED AT 17:09:34 ON 28 MAY 2004
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FILE LAST UPDATED:           27 MAY 2004       <20040527/UP>
MOST RECENT DERWENT UPDATE:     200434          <200434/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
    http://thomsonderwent.com/coverage/latestupdates/            <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
    GUIDES, PLEASE VISIT:
    http://thomsonderwent.com/support/userguides/                <<<

>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT
    DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX
    FIRST VIEW - FILE WPIFV. FREE CONNECT HOUR UNTIL 1 MAY 2004.
    FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv  <<<

>>> NEW! IMPROVE YOUR LITIGATION CHECKING AND INFRINGEMENT
    MONITORING WITH LITALERT. FIRST ACCESS TO RECORDS OF IP
    LAWSUITS FILED IN THE 94 US DISTRICT COURTS SINCE 1973.
    FOR FURTHER DETAILS:
    http://www.thomsonscientific.com/litalert                    <<<

>>> THE DISPLAY LAYOUT HAS BEEN CHANGED TO ACCOMODATE THE
    NEW FORMAT GERMAN PATENT APPLICATION AND PUBLICATION
    NUMBERS. SEE ALSO:
    http://www.stn-international.de/archive/stnews/news0104.pdf <<<

>>> SINCE THE FILE HAD NOT BEEN UPDATED BETWEEN APRIL 12-16
    THERE WAS NO WEEKLY SDI RUN  <<<
```

Searched by Barb O'Bryen, STIC 571-272-2518

```
L106          640 SEA FILE=WPIDS ABB=ON  PYRIDOXAL OR PYRIDOXAMIN#
L107         3295 SEA FILE=WPIDS ABB=ON  ANTIPLATELET OR ANTI PLATELET OR
                  (PLATELET AGGREGATION)(2A)INHIBIT?
L108         7773 SEA FILE=WPIDS ABB=ON  ANTITHROMB? OR ANTI THROMB? OR THROMBOLY
                  TIC?
L109         7391 SEA FILE=WPIDS ABB=ON  ASPIRIN OR HEPARIN OR HIRUDIN OR
                  WARFARIN
L110        10296 SEA FILE=WPIDS ABB=ON  (EMBOLI? OR THROMBOEMBOLI? OR THROMBOS!S
                   )
L111         5557 SEA FILE=WPIDS ABB=ON  ((REDUC? OR INHIBIT? OR PREVENT? OR
                  DECREAS?)(3A)CLOT?)
L112            9 SEA FILE=WPIDS ABB=ON  L106 AND (L107 OR L108 OR L109) AND
                  (L110 OR L111)


=> dup rem l113,l65,l115,l114,l74,l112
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FILE 'USPATFULL' ENTERED AT 17:10:27 ON 28 MAY 2004
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FILE 'MEDLINE' ENTERED AT 17:10:27 ON 28 MAY 2004

FILE 'EMBASE' ENTERED AT 17:10:27 ON 28 MAY 2004
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FILE 'WPIDS' ENTERED AT 17:10:27 ON 28 MAY 2004
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PROCESSING COMPLETED FOR L113
PROCESSING COMPLETED FOR L65
PROCESSING COMPLETED FOR L115
PROCESSING COMPLETED FOR L114
PROCESSING COMPLETED FOR L74
PROCESSING COMPLETED FOR L112
L116           27 DUP REM L113 L65 L115 L114 L74 L112 (3 DUPLICATES REMOVED)
                  ANSWERS '1-4' FROM FILE CAPLUS
                  ANSWERS '5-11' FROM FILE USPATFULL
                  ANSWERS '12-15' FROM FILE MEDLINE
                  ANSWERS '16-17' FROM FILE EMBASE
                  ANSWERS '18-19' FROM FILE TOXCENTER
                  ANSWERS '20-27' FROM FILE WPIDS

=> d ibib ed abs hitstr 1-11; d iall 12-27; fil hom

L116 ANSWER 1 OF 27  CAPLUS  COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2004:41126  CAPLUS
DOCUMENT NUMBER:          140:71072
TITLE:                    Preparation of pyridoxine and pyridoxal analogs and
                          their therapeutic uses
INVENTOR(S):              Haque, Wasimul
PATENT ASSIGNEE(S):       Can.
SOURCE:                   U.S. Pat. Appl. Publ., 31 pp., Cont.-in-part of U.S.
                          6,548,519.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
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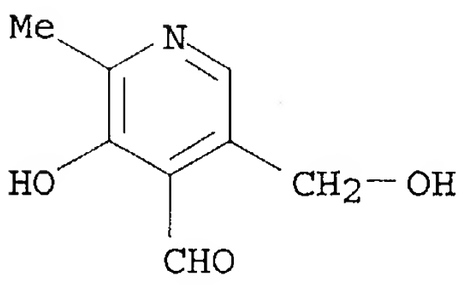
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

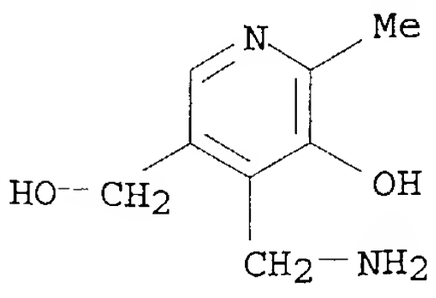
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2004010015 | A1 | 20040115 | US 2003-411552 | 20030410 |
| US 6417204 | B1 | 20020709 | US 2001-900718 | 20010706 |
| US 6548519 | B1 | 20030415 | US 2002-147263 | 20020515 |

PRIORITY APPLN. INFO.: US 2001-900718 A2 20010706
US 2002-147263 A2 20020515
US 2000-216907P P 20000707
OTHER SOURCE(S): CASREACT 140:71072; MARPAT 140:71072
ED Entered STN: 18 Jan 2004
AB The invention provides pyridoxal and pyridoxine analogs, pharmaceutical compns. contg. pyridoxine and pyridoxal analogs, and methods of administering pharmaceutical compns. contg. a therapeutically effective amt. of at least one of these analogs. In accordance with the present invention, the pyridoxal and pyridoxine analogs can be used in the treatment or prevention of heparin induced thrombocytopenia (HIT), stroke, and ischemia, and in the treatment of symptoms thereof. The the pyridoxal and pyridoxine analogs can be used in neuroprotection.
IT **9005-49-6**, Heparin, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(heparin induced thrombocytopenia treatment; prepn. of pyridoxine and pyridoxal analogs and their therapeutic uses)
RN 9005-49-6 CAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **66-72-8DP**, Pyridoxal, analogs **85-87-0DP**, Pyridoxamine, analogs
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyridoxine and pyridoxal analogs and their therapeutic uses)
RN 66-72-8 CAPLUS
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-5-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)

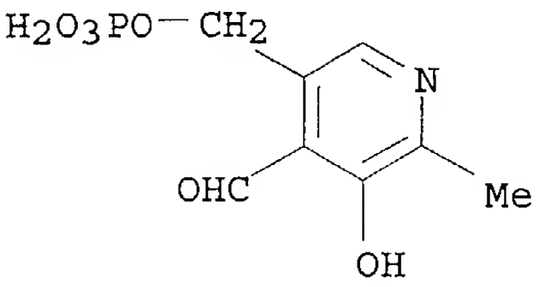



RN 85-87-0 CAPLUS
CN 3-Pyridinemethanol, 4-(aminomethyl)-5-hydroxy-6-methyl- (9CI) (CA INDEX NAME)



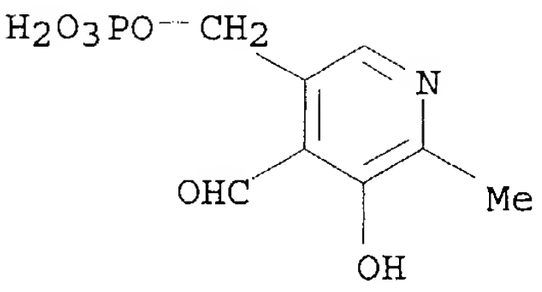

Searched by Barb O'Bryen, STIC 571-272-2518

IT **54-47-7**, Pyridoxal 5'-phosphate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of pyridoxine and pyridoxal analogs and their therapeutic uses)
RN 54-47-7 CAPLUS
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]- (9CI) (CA INDEX NAME)



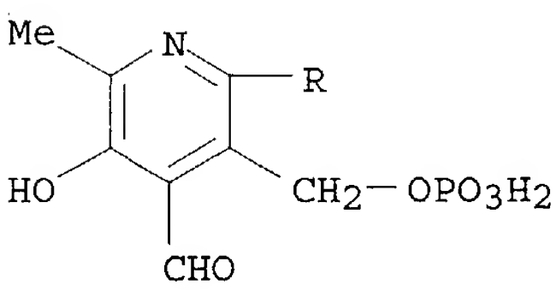

L116 ANSWER 2 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:60856 CAPLUS
DOCUMENT NUMBER: 132:246253
TITLE: The novel pyridoxal-5'-phosphate derivative PPNDS potently antagonizes activation of P2X1 receptors
AUTHOR(S): Lambrecht, G.; Rettinger, J.; Baumert, H. G.; Czeche, S.; Damer, S.; Ganso, M.; Hildebrandt, C.; Niebel, B.; Spatz-Kumbel, G.; Schmalzing, G.; Mutschler, E.
CORPORATE SOURCE: Biocentre Niederursel, Department of Pharmacology, University of Frankfurt, Frankfurt, D-60439, Germany
SOURCE: European Journal of Pharmacology (2000), 387(3), R19-R21
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 26 Jan 2000
AB Pyridoxal-5'-phosphate-6-(2'-naphthylazo-6'-nitro-4',8'-disulfonate) (PPNDS) potently antagonized P2X1 receptor-mediated responses in rat vas deferens (pKB=7.43) and Xenopus laevis oocytes (pIC50=7.84). It showed lower (up to 20,000-fold) inhibitory potency on ecto-nucleotidase in Xenopus oocytes and on P2Y1 receptors in guinea-pig ileum (pA2=6.13). PPNDS did not interact with .alpha.1A-adrenoceptors, adenosine A1 and A2B, histamine H1 and muscarinic M3 receptors. Thus, PPNDS is a novel, specific P2 receptor antagonist and represents the pyridoxal-5'-phosphate deriv. with the highest potency at P2X1 receptors.

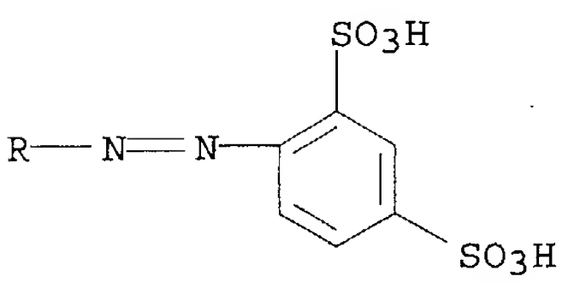
IT **54-47-7D**, Pyridoxal-5'-phosphate, deriv. **149017-66-3**, PPADS
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(the novel pyridoxal-5'-phosphate deriv. PPNDS, potent P2X1 receptor antagonist)
RN 54-47-7 CAPLUS
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]- (9CI) (CA INDEX NAME)




Searched by Barb O'Bryen, STIC 571-272-2518

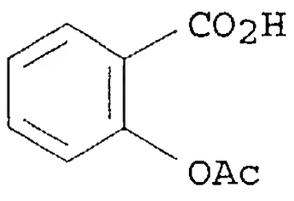
RN 149017-66-3 CAPLUS
CN 1,3-Benzenedisulfonic acid, 4-[[4-formyl-5-hydroxy-6-methyl-3-[(phosphonooxy)methyl]-2-pyridinyl]azo]- (9CI) (CA INDEX NAME)



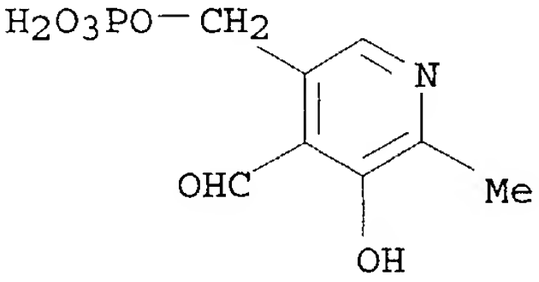




REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

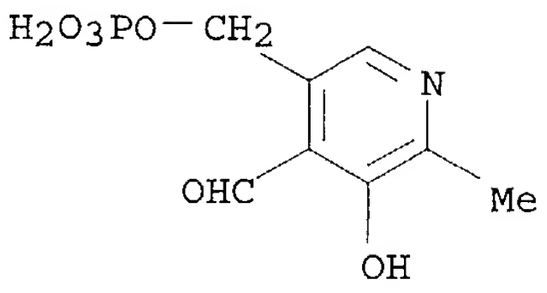
L116 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:597060 CAPLUS
DOCUMENT NUMBER: 109:197060
TITLE: Gastric emptying rates of drug preparations. I. Effects of size of dosage forms, food and species on gastric emptying rates
AUTHOR(S): Kaniwa, Nahoko; Aoyagi, Nobuo; Ogata, Hiroyasu; Ejima, Akira
CORPORATE SOURCE: Drugs Div., Natl. Inst. Hyg. Sci., Tokyo, 158, Japan
SOURCE: Journal of Pharmacobio-Dynamics (1988), 11(8), 563-70
CODEN: JOPHDQ; ISSN: 0386-846X
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 25 Nov 1988
AB The gastric emptying rates of oral dosage forms of different sizes were studied in humans and beagle dogs measuring of marker drugs such as acetaminophen, aspirin, and pyridoxal phosphate in plasma or urine. The marker drugs, except acetaminophen, were contained in enteric-coated granules or tablets which did not dissolve in the stomach but dissolved rapidly in the upper intestine. The gastric emptying rate of a dosage form of smaller size was faster than that of a larger size. The gastric emptying rates of dosage forms with different sizes did not correlate with each other inter-individually. The gastric emptying rates of dosage forms of any size were delayed when drugs were administered after taking a meal. The gastric emptying rates of dosage forms were extremely prolonged in beagle dogs after drug administration postprandially, and this restricted the use of beagle dogs as an animal model in bioavailability tests.
IT **50-78-2**, Aspirin **54-47-7**, Pyridoxal phosphate
RL: BIOL (Biological study)
(oral dosage forms contg., gastric emptying of, in humans and lab. animals, dosage size and food effect on)
RN 50-78-2 CAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



RN 54-47-7 CAPLUS
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]-
(9CI) (CA INDEX NAME)



L116 ANSWER 4 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1986:441638 CAPLUS
DOCUMENT NUMBER: 105:41638
TITLE: Effect of oral vitamin B6 supplementation on in vitro platelet aggregation
AUTHOR(S): Schoene, Norberta W.; Chanmugam, Prithiva; Reynolds, Robert D.
CORPORATE SOURCE: Beltsville Hum. Nutr. Res. Cent., US Dep. Agric., Beltsville, MD, USA
SOURCE: American Journal of Clinical Nutrition (1986), 43(5), 825-30
CODEN: AJCNAC; ISSN: 0002-9165
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 09 Aug 1986
AB A randomized, double-blind study was conducted with 12 healthy adult males to det. the effects of oral pyridoxine-HCl [58-56-0] supplementation on in vitro platelet aggregation. Following a 4-wk baseline period, half the subjects received 100 mg/day of pyridoxine-HCl, and the remaining subjects received a placebo for 6 wk. In vitro platelet responses to ADP and collagen and the plasma pyridoxal 5'-phosphate (PLP) **[54-47-7]** concns. were measured at biweekly intervals. Plasma PLP concns. increased significantly for those receiving the vitamin B6 compared to baseline values or compared to those receiving the placebo; however, there was no significant effect of increased levels of plasma PLP on collagen-stimulated platelet aggregation and only a slight effect on ADP-stimulated aggregation. Acute administration of 100 mg pyridoxine-HCl failed to alter the in vitro response of platelets to either ADP or collagen. Reevaluation of conclusions based solely on in vitro studies suggesting the use of pyridoxine as an effective in vivo antithrombotic agent may be warranted.
IT **54-47-7**
RL: BIOL (Biological study)
(of blood plasma, platelet aggregation in relation to, in men)
RN 54-47-7 CAPLUS
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]-
(9CI) (CA INDEX NAME)



L116 ANSWER 5 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2004:51514 USPATFULL
TITLE: Treatment of cardiovascular and related pathologies
INVENTOR(S): Sethi, Rajat, Winnipeg, CANADA
Haque, Wasimul, Edmonton, CANADA
PATENT ASSIGNEE(S): Medicure International Inc. (non-U.S. corporation)

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2004038945 | A1 | 20040226 |
| APPLICATION INFO.: | US 2003-639948 | A1 | 20030812 (10) |

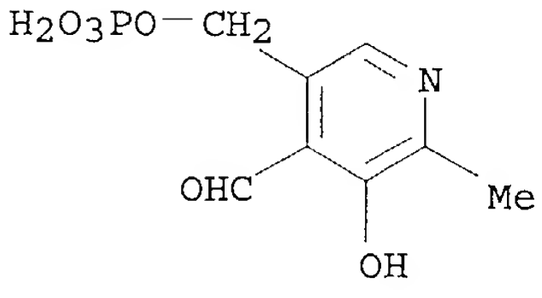
RELATED APPLN. INFO.: Division of Ser. No. US 2000-645237, filed on 24 Aug 2000, PENDING

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1999-150415P | 19990824 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MERCHANT & GOULD PC, P.O. BOX 2903, MINNEAPOLIS, MN, 55402-0903
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 34 Drawing Page(s)
LINE COUNT: 1172
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods for treating cardiovascular and related diseases such as hypertrophy are described. The methods are directed to **concurrently** administering a compound such as pyridoxal-5'-phosphate, pyridoxamine, pyridoxal, or a 3-acylated pyridoxal analogue with a therapeutic cardiovascular compound.

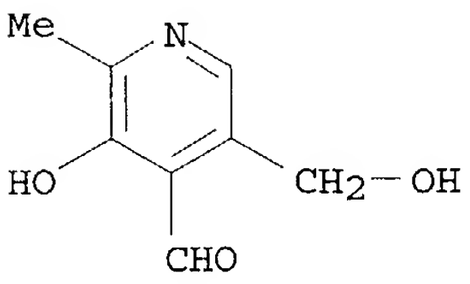
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **54-47-7**, Pyridoxal 5'-phosphate **66-72-8**, Pyridoxal **66-72-8D**, Pyridoxal, acylated analogs **85-87-0**, Pyridoxamine
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)
RN 54-47-7 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]- (9CI) (CA INDEX NAME)



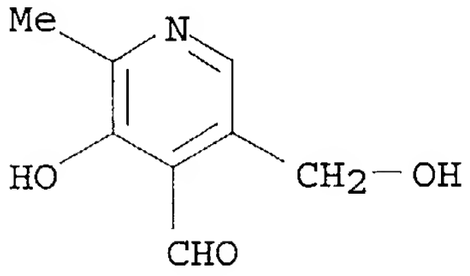
RN 66-72-8 USPATFULL

Searched by Barb O'Bryen, STIC 571-272-2518

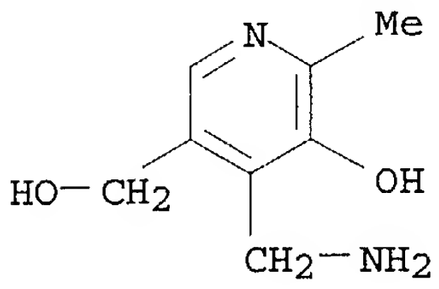
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-5-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)



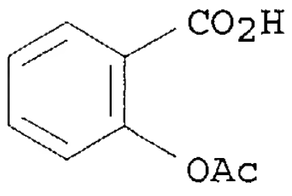

RN 66-72-8 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-5-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)




RN 85-87-0 USPATFULL
CN 3-Pyridinemethanol, 4-(aminomethyl)-5-hydroxy-6-methyl- (9CI) (CA INDEX NAME)




IT **50-78-2**, **Aspirin** **9005-49-6**, **Heparin**
, biological studies **149017-66-3**
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)
RN 50-78-2 USPATFULL
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)

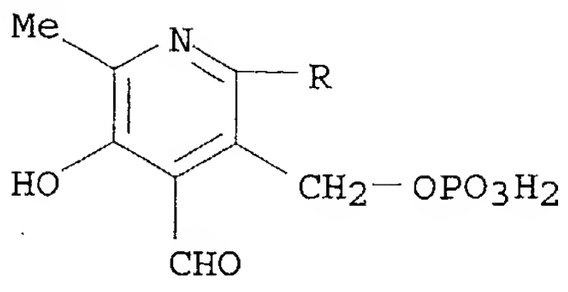


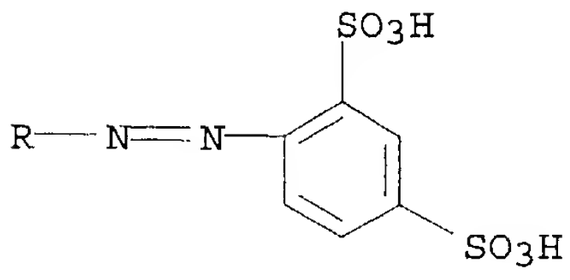

RN 9005-49-6 USPATFULL
CN Heparin (8CI, 9CI) (CA INDEX NAME)

**STRUCTURE DIAGRAM IS NOT AVAILABLE**

RN 149017-66-3 USPATFULL
CN 1,3-Benzenedisulfonic acid, 4-[[4-formyl-5-hydroxy-6-methyl-3-[(phosphonooxy)methyl]-2-pyridinyl]azo]- (9CI) (CA INDEX NAME)

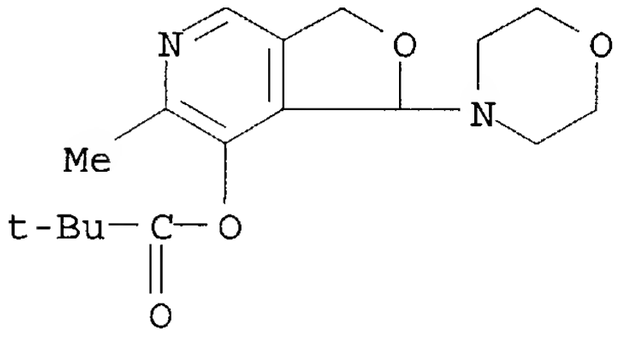
Searched by Barb O'Bryen, STIC 571-272-2518



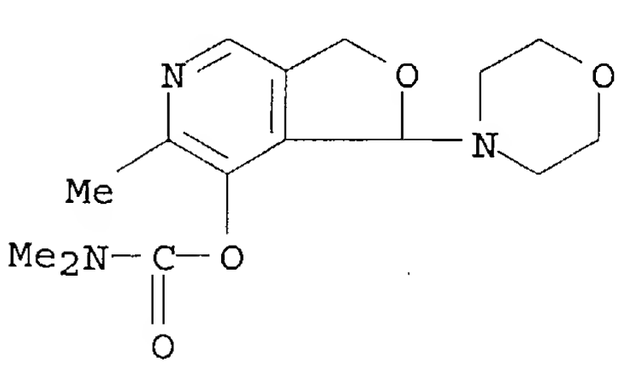




IT **292611-24-6P 292611-25-7P 292611-26-8P**
**292611-32-6P 292611-36-0P 292611-37-1P**
**320591-83-1P**
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)

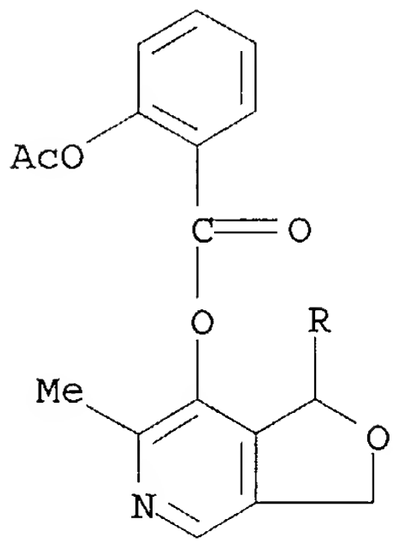
RN 292611-24-6 USPATFULL
CN Propanoic acid, 2,2-dimethyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

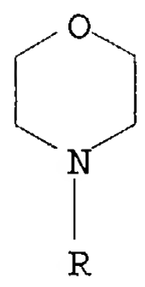



RN 292611-25-7 USPATFULL
CN Carbamic acid, dimethyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

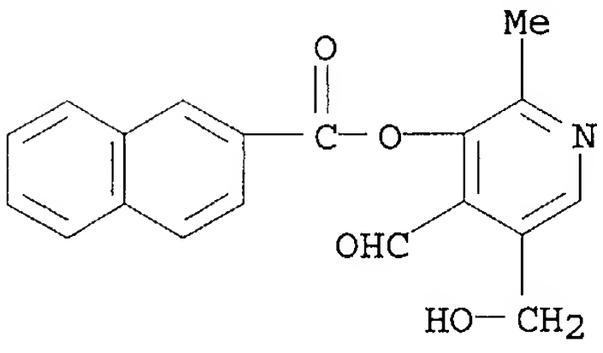



RN 292611-26-8 USPATFULL
CN Benzoic acid, 2-(acetyloxy)-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)



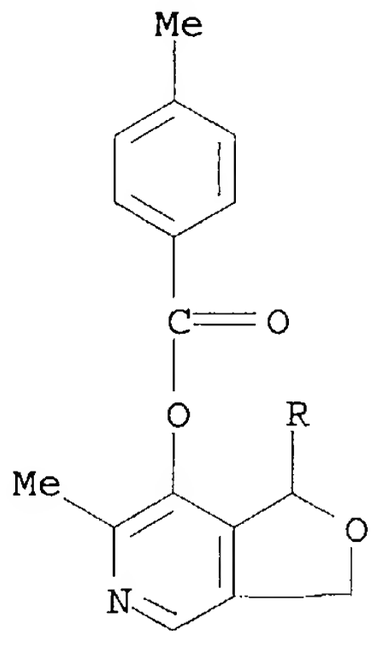


RN 292611-32-6 USPATFULL
CN 2-Naphthalenecarboxylic acid, 4-formyl-5-(hydroxymethyl)-2-methyl-3-pyridinyl ester (9CI) (CA INDEX NAME)

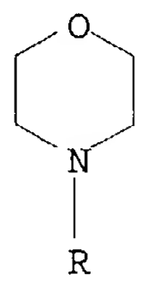


RN 292611-36-0 USPATFULL
CN Benzoic acid, 4-methyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

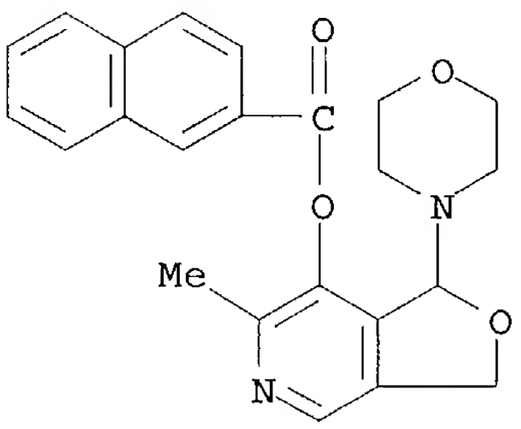




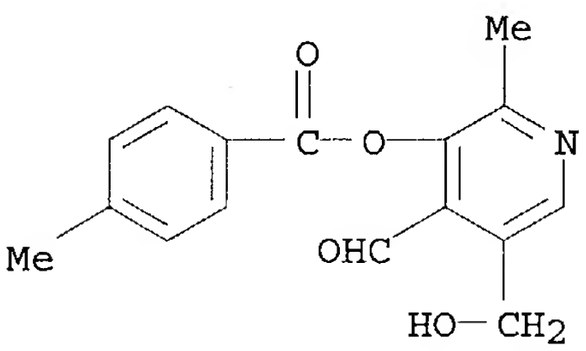
PAGE 2-A



RN 292611-37-1 USPATFULL
CN 2-Naphthalenecarboxylic acid, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)



RN 320591-83-1 USPATFULL
CN Benzoic acid, 4-methyl-, 4-formyl-5-(hydroxymethyl)-2-methyl-3-pyridinyl ester (9CI) (CA INDEX NAME)



L116 ANSWER 6 OF 27 USPATFULL on STN

ACCESSION NUMBER: 2004:45000 USPATFULL
TITLE: Treatment of cardiovascular and related pathologies
INVENTOR(S): Sethi, Rajat, Winnipeg, CANADA
Haque, Wasimul, Edmonton, CANADA
PATENT ASSIGNEE(S): Medicure International Inc. (non-U.S. corporation)

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2004033993 | A1 | 20040219 |
| APPLICATION INFO.: | US 2003-639955 | A1 | 20030812 (10) |

RELATED APPLN. INFO.: Division of Ser. No. US 2000-645237, filed on 24 Aug 2000, PENDING

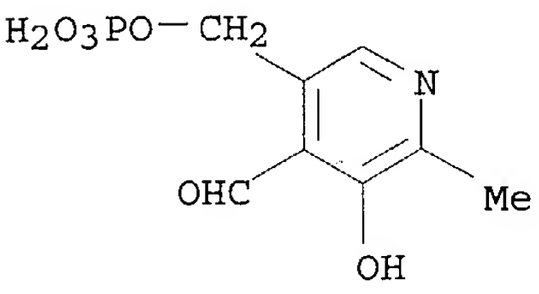
| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1999-150415P | 19990824 (60) |

DOCUMENT TYPE: Utility

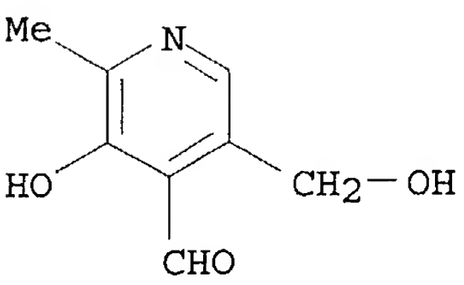
Searched by Barb O'Bryen, STIC 571-272-2518

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Attention of Anna M. Nelson, MERCHANT & GOULD P.C., P.O. Box 2903, Minneapolis, MN, 55402-0903
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 34 Drawing Page(s)
LINE COUNT: 1272
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for treating cardiovascular and related diseases such as ischemia, ischemia reperfusion injuries, and myocardial ischemia, are described. The methods are directed to **concurrently** administering a compound such as pyridoxal-5'-phosphate, pyridoxamine, pyridoxal, or a 3-acylated pyridoxal analogue with a therapeutic cardiovascular compound.

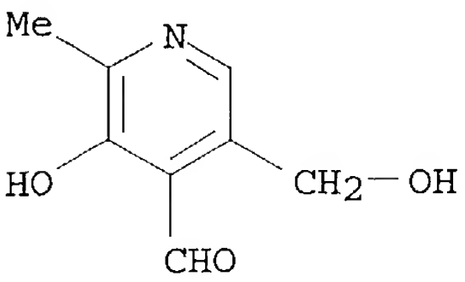
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **54-47-7**, Pyridoxal 5'-phosphate **66-72-8**, Pyridoxal **66-72-8D**, Pyridoxal, acylated analogs **85-87-0**, Pyridoxamine
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)
RN 54-47-7 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]- (9CI) (CA INDEX NAME)




RN 66-72-8 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-5-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)



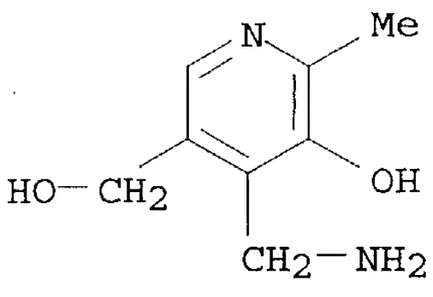

RN 66-72-8 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-5-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)



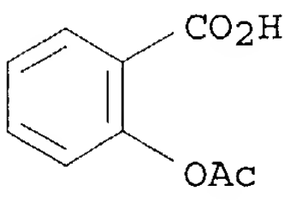

RN 85-87-0 USPATFULL
CN 3-Pyridinemethanol, 4-(aminomethyl)-5-hydroxy-6-methyl- (9CI) (CA INDEX

Searched by Barb O'Bryen, STIC 571-272-2518

NAME)

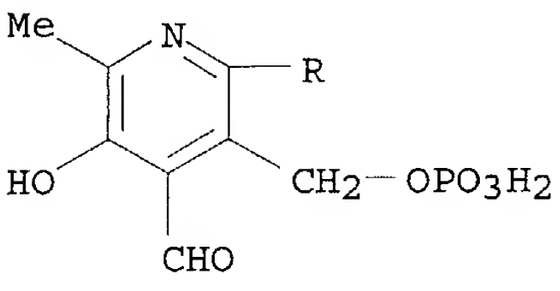


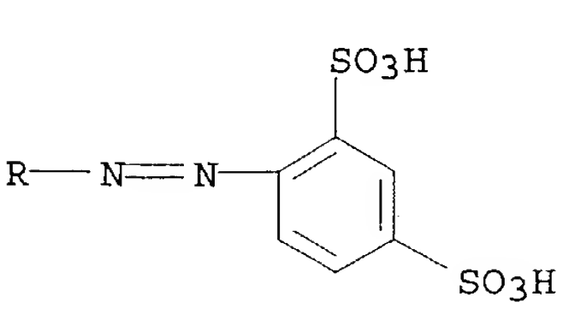
IT **50-78-2, Aspirin 9005-49-6, Heparin**
, biological studies **149017-66-3**
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)
RN 50-78-2 USPATFULL
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



RN 9005-49-6 USPATFULL
CN Heparin (8CI, 9CI) (CA INDEX NAME)

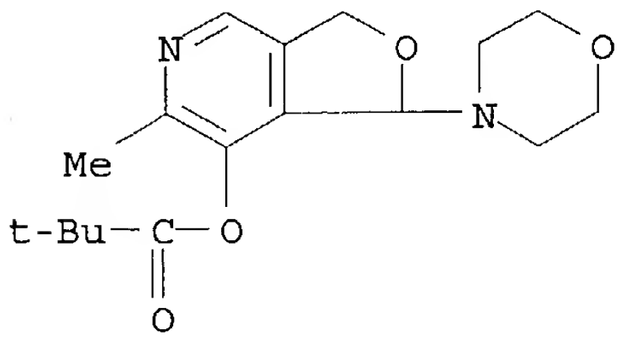
**STRUCTURE DIAGRAM IS NOT AVAILABLE**
RN 149017-66-3 USPATFULL
CN 1,3-Benzenedisulfonic acid, 4-[[4-formyl-5-hydroxy-6-methyl-3-[(phosphonooxy)methyl]-2-pyridinyl]azo]- (9CI) (CA INDEX NAME)



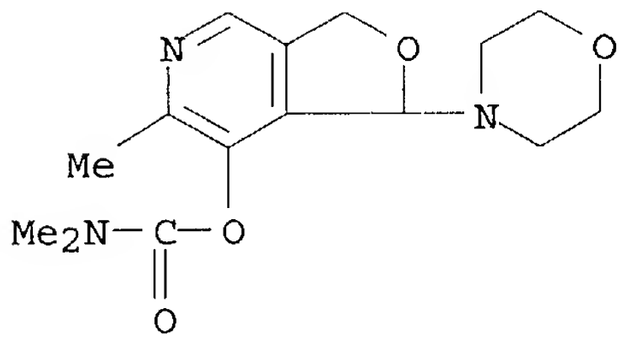


IT **292611-24-6P 292611-25-7P 292611-26-8P**
**292611-32-6P 292611-36-0P 292611-37-1P**
**320591-83-1P**
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)
RN 292611-24-6 USPATFULL
CN Propanoic acid, 2,2-dimethyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

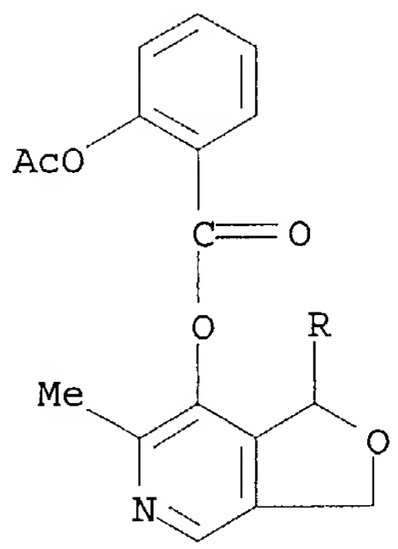
Searched by Barb O'Bryen, STIC 571-272-2518

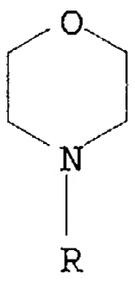


RN 292611-25-7 USPATFULL
CN Carbamic acid, dimethyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

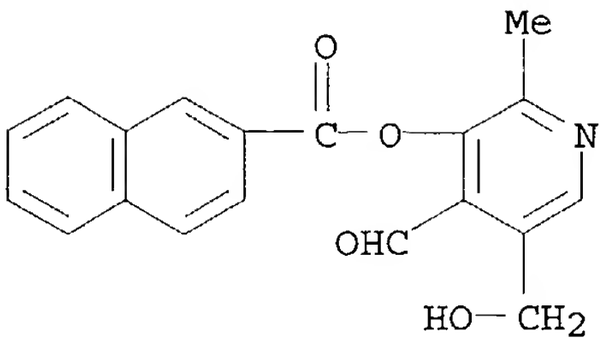


RN 292611-26-8 USPATFULL
CN Benzoic acid, 2-(acetyloxy)-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)



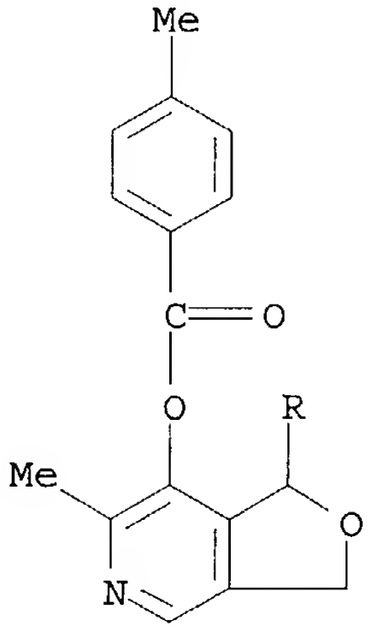


RN 292611-32-6 USPATFULL
CN 2-Naphthalenecarboxylic acid, 4-formyl-5-(hydroxymethyl)-2-methyl-3-pyridinyl ester (9CI) (CA INDEX NAME)

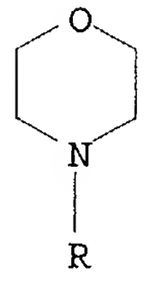


RN 292611-36-0 USPATFULL
CN Benzoic acid, 4-methyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

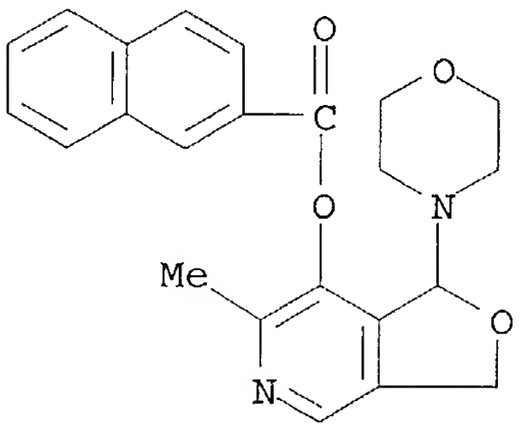
PAGE 1-A



PAGE 2-A

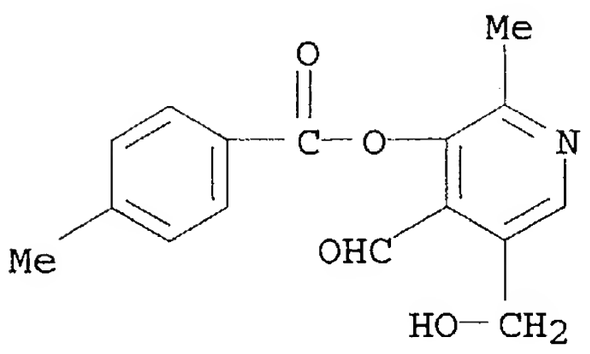


RN 292611-37-1 USPATFULL
CN 2-Naphthalenecarboxylic acid, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)



Searched by Barb O'Bryen, STIC 571-272-2518

RN 320591-83-1 USPATFULL
CN Benzoic acid, 4-methyl-, 4-formyl-5-(hydroxymethyl)-2-methyl-3-pyridinyl ester (9CI) (CA INDEX NAME)




L116 ANSWER 7 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2004:44999 USPATFULL
TITLE: Treatment of cardiovascular and related pathologies
INVENTOR(S): Sethi, Rajat, Winnipeg, CANADA
Haque, Wasimul, Edmonton, CANADA
PATENT ASSIGNEE(S): Medicure International Inc., West Indies, BARBADOS (non-U.S. corporation)

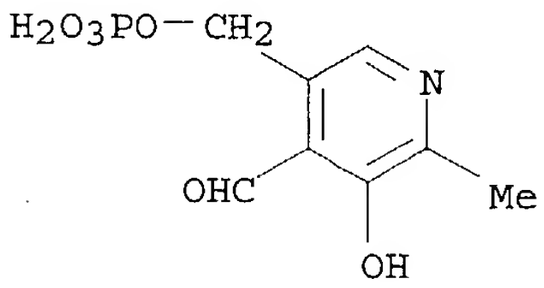
| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2004033992 | A1 | 20040219 |
| APPLICATION INFO.: | US 2003-639950 | A1 | 20030812 (10) |

RELATED APPLN. INFO.: Division of Ser. No. US 2000-645237, filed on 24 Aug 2000, PENDING

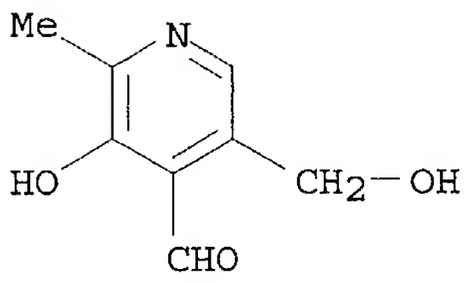
| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1999-150415P | 19990824 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MERCHANT & GOULD PC, P.O. BOX 2903, MINNEAPOLIS, MN, 55402-0903
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 34 Drawing Page(s)
LINE COUNT: 1178
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for treating cardiovascular and related diseases such congestive heart failure are described. The methods are directed to **concurrently** administering a compound such as pyridoxal-5'-phosphate, pyridoxamine, pyridoxal, or a 3-acylated pyridoxal analogue with a therapeutic cardiovascular compound.

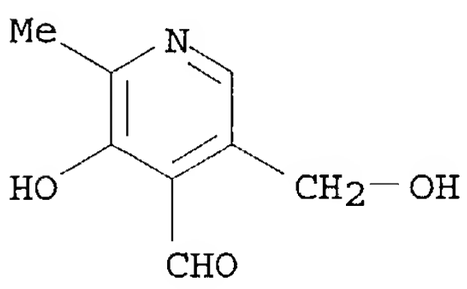
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **54-47-7**, Pyridoxal 5'-phosphate **66-72-8**, Pyridoxal **66-72-8D**, Pyridoxal, acylated analogs **85-87-0**, Pyridoxamine
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)
RN 54-47-7 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]- (9CI) (CA INDEX NAME)



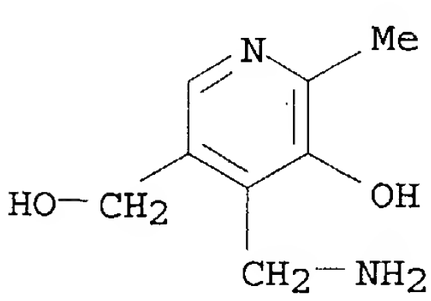
RN 66-72-8 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-5-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)



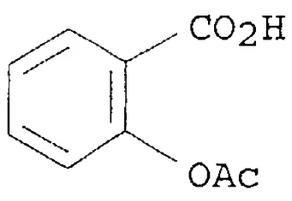
RN 66-72-8 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-5-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)



RN 85-87-0 USPATFULL
CN 3-Pyridinemethanol, 4-(aminomethyl)-5-hydroxy-6-methyl- (9CI) (CA INDEX NAME)



IT **50-78-2**, **Aspirin** **9005-49-6**, **Heparin**
, biological studies **149017-66-3**
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)
RN 50-78-2 USPATFULL
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)

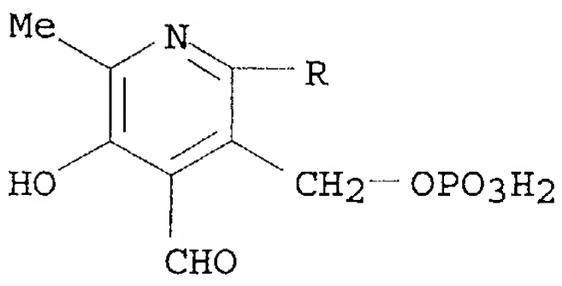


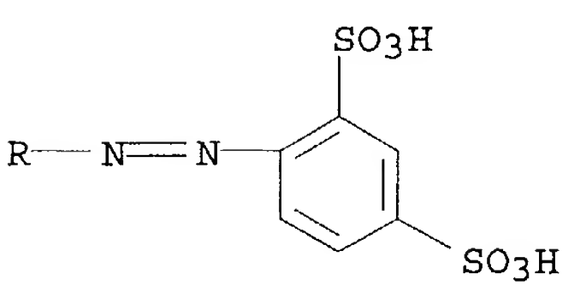
Searched by Barb O'Bryen, STIC 571-272-2518

RN 9005-49-6 USPATFULL
CN Heparin (8CI, 9CI) (CA INDEX NAME)

**STRUCTURE DIAGRAM IS NOT AVAILABLE**

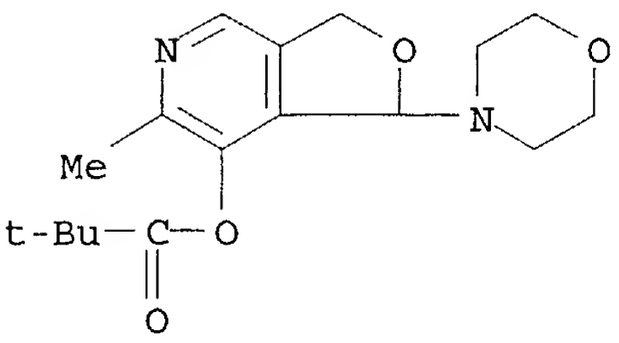
RN 149017-66-3 USPATFULL
CN 1,3-Benzenedisulfonic acid, 4-[[4-formyl-5-hydroxy-6-methyl-3-[(phosphonooxy)methyl]-2-pyridinyl]azo]- (9CI) (CA INDEX NAME)



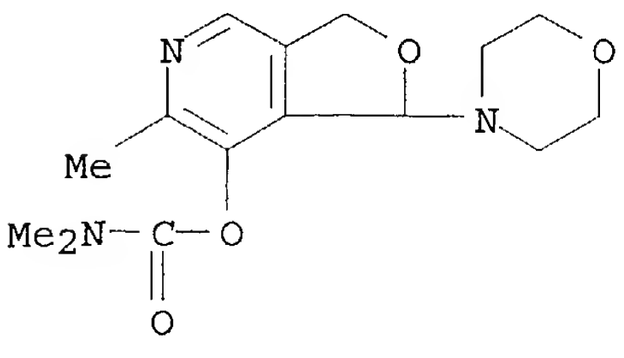




IT **292611-24-6P 292611-25-7P 292611-26-8P**
**292611-32-6P 292611-36-0P 292611-37-1P**
**320591-83-1P**
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)

RN 292611-24-6 USPATFULL
CN Propanoic acid, 2,2-dimethyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

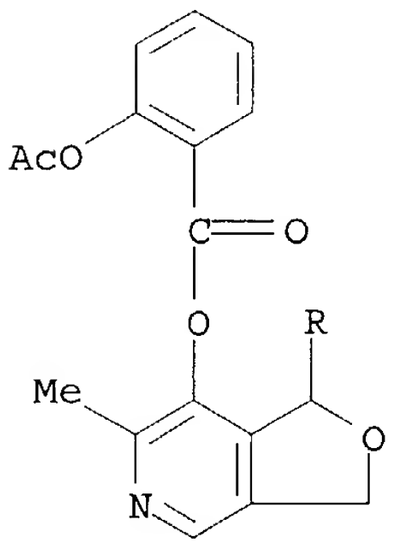


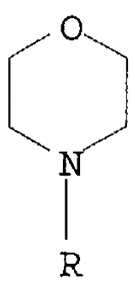

RN 292611-25-7 USPATFULL
CN Carbamic acid, dimethyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)



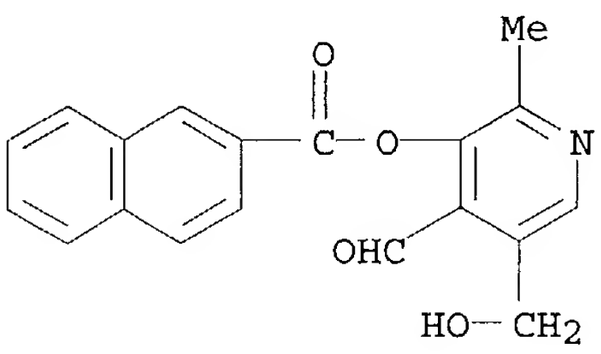

Searched by Barb O'Bryen, STIC 571-272-2518

RN 292611-26-8 USPATFULL
CN Benzoic acid, 2-(acetyloxy)-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)



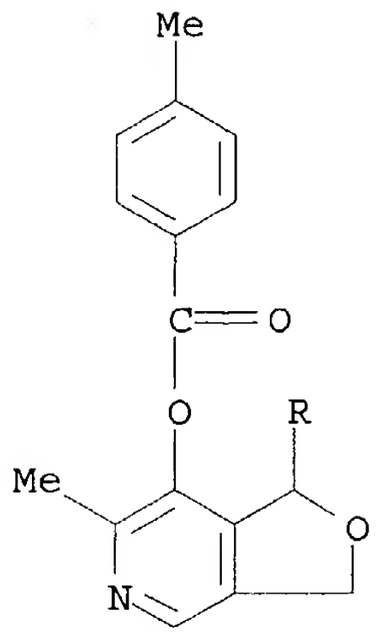




RN 292611-32-6 USPATFULL
CN 2-Naphthalenecarboxylic acid, 4-formyl-5-(hydroxymethyl)-2-methyl-3-pyridinyl ester (9CI) (CA INDEX NAME)

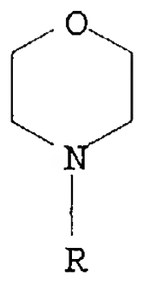



RN 292611-36-0 USPATFULL
CN Benzoic acid, 4-methyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

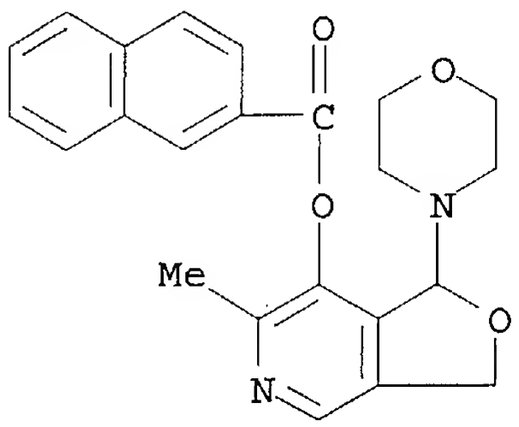
PAGE 1-A



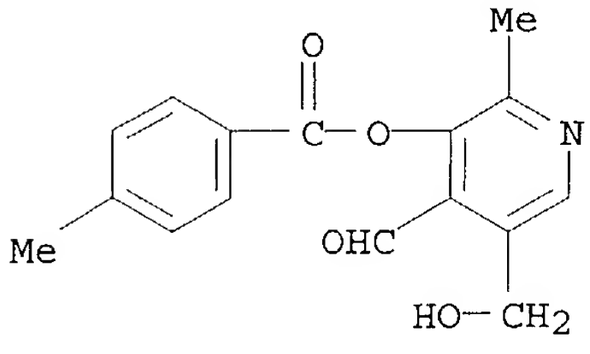
PAGE 2-A



RN 292611-37-1 USPATFULL
CN 2-Naphthalenecarboxylic acid, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)



RN 320591-83-1 USPATFULL
CN Benzoic acid, 4-methyl-, 4-formyl-5-(hydroxymethyl)-2-methyl-3-pyridinyl ester (9CI) (CA INDEX NAME)



L116 ANSWER 8 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2004:44998 USPATFULL
TITLE: Treating of cardiovascular and related pathologies
INVENTOR(S): Sethi, Rajat, Winnipeg, CANADA
Haque, Wasimul, Edmonton, CANADA
PATENT ASSIGNEE(S): Medicure International Inc. (non-U.S. corporation)

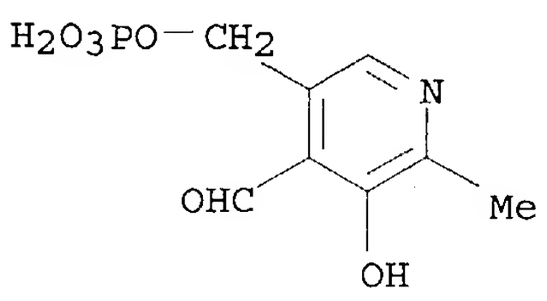
| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2004033991 | A1 | 20040219 |
| APPLICATION INFO.: | US 2003-639949 | A1 | 20030812 (10) |

RELATED APPLN. INFO.: Division of Ser. No. US 2000-645237, filed on 24 Aug 2000, PENDING

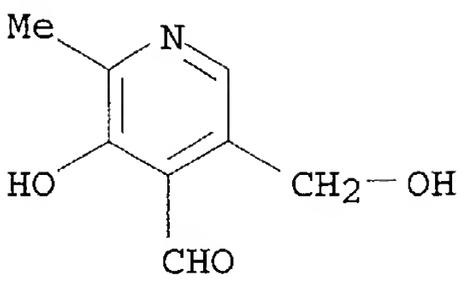
| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1999-150415P | 19990824 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MERCHANT & GOULD PC, P.O. BOX 2903, MINNEAPOLIS, MN, 55402-0903
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 34 Drawing Page(s)
LINE COUNT: 1167
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for treating cardiovascular and related diseases such as blood clots are described. The methods are directed to **concurrently** administering a compound such as pyridoxal-5'-phosphate, pyridoxamine, pyridoxal, or a 3-acylated pyridoxal analogue with a therapeutic cardiovascular compound.

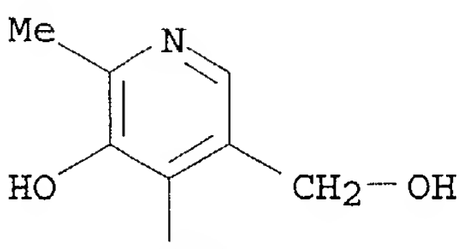
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **54-47-7**, Pyridoxal 5'-phosphate **66-72-8**, Pyridoxal **66-72-8D**, Pyridoxal, acylated analogs **85-87-0**, Pyridoxamine
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)
RN 54-47-7 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]- (9CI) (CA INDEX NAME)



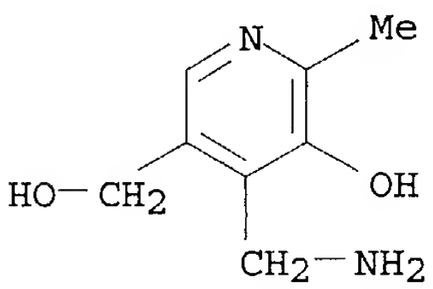

RN 66-72-8 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-5-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)



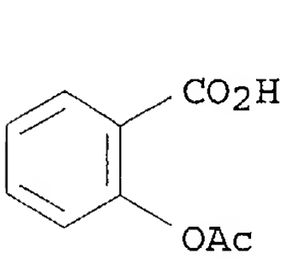
RN 66-72-8 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-5-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)



RN 85-87-0 USPATFULL
CN 3-Pyridinemethanol, 4-(aminomethyl)-5-hydroxy-6-methyl- (9CI) (CA INDEX NAME)



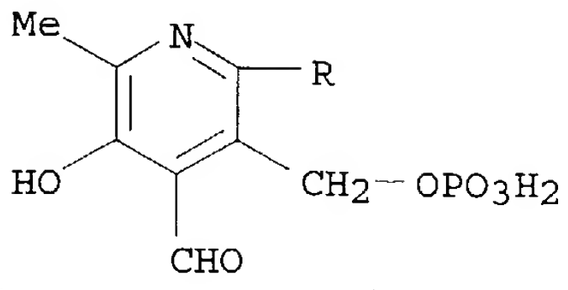
IT **50-78-2**, **Aspirin** **9005-49-6**, **Heparin**
, biological studies **149017-66-3**
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)
RN 50-78-2 USPATFULL
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)

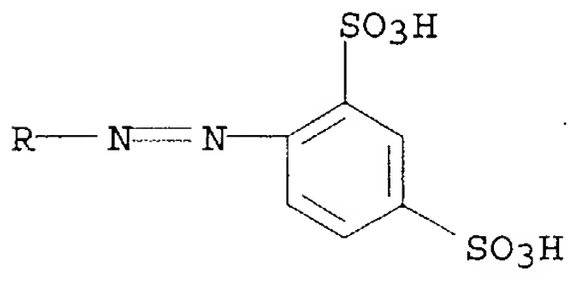


RN 9005-49-6 USPATFULL
CN Heparin (8CI, 9CI) (CA INDEX NAME)

**STRUCTURE DIAGRAM IS NOT AVAILABLE**

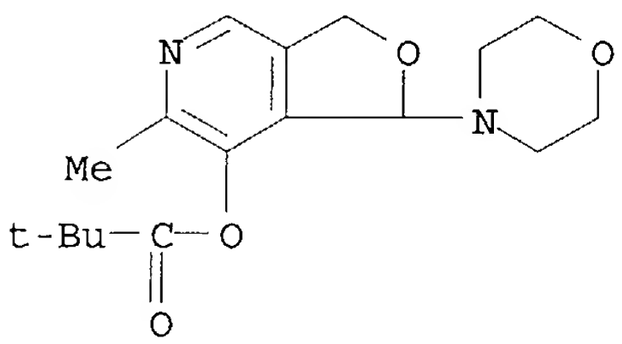
RN 149017-66-3 USPATFULL
CN 1,3-Benzenedisulfonic acid, 4-[[4-formyl-5-hydroxy-6-methyl-3-[(phosphonooxy)methyl]-2-pyridinyl]azo]- (9CI) (CA INDEX NAME)



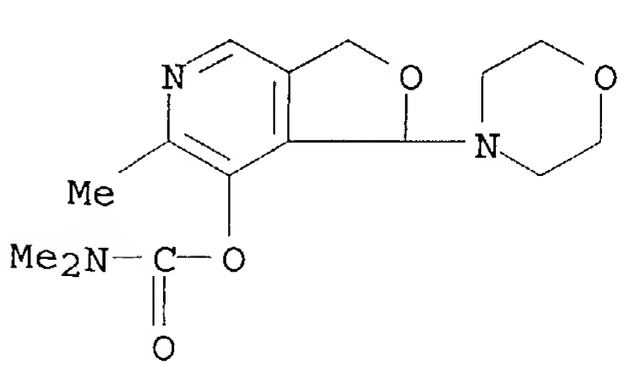


IT **292611-24-6P 292611-25-7P 292611-26-8P**
**292611-32-6P 292611-36-0P 292611-37-1P**
**320591-83-1P**
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)

RN 292611-24-6 USPATFULL
CN Propanoic acid, 2,2-dimethyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

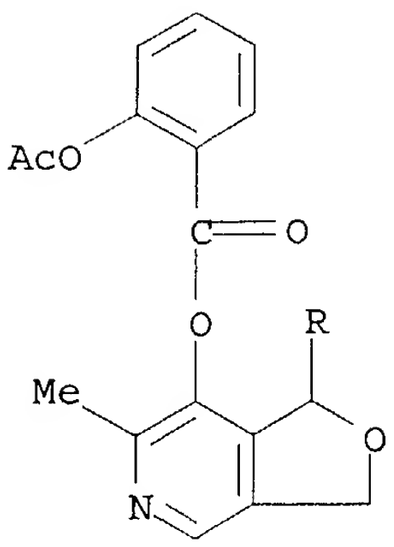


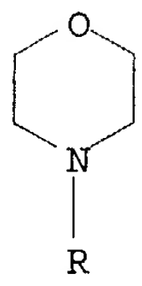
RN 292611-25-7 USPATFULL
CN Carbamic acid, dimethyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)



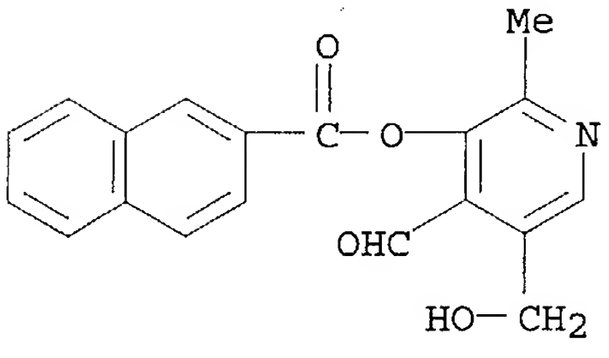
RN 292611-26-8 USPATFULL
CN Benzoic acid, 2-(acetyloxy)-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

Searched by Barb O'Bryen, STIC 571-272-2518



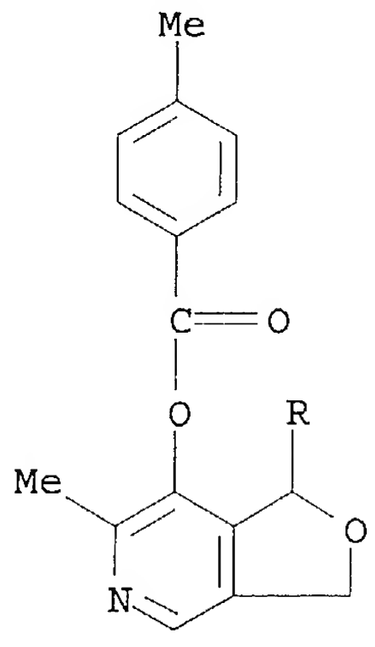


RN 292611-32-6 USPATFULL
CN 2-Naphthalenecarboxylic acid, 4-formyl-5-(hydroxymethyl)-2-methyl-3-pyridinyl ester (9CI) (CA INDEX NAME)



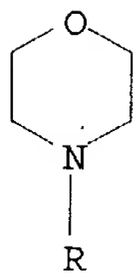
RN 292611-36-0 USPATFULL
CN Benzoic acid, 4-methyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

PAGE 1-A

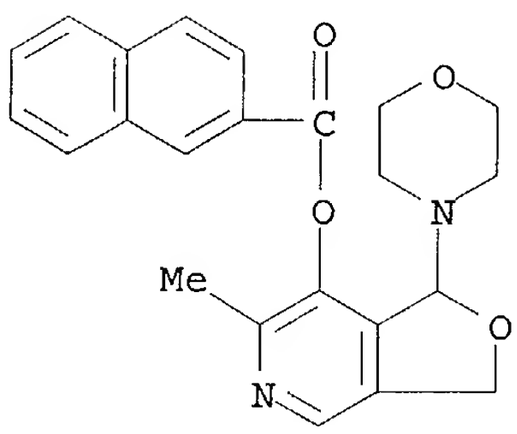


Searched by Barb O'Bryen, STIC 571-272-2518

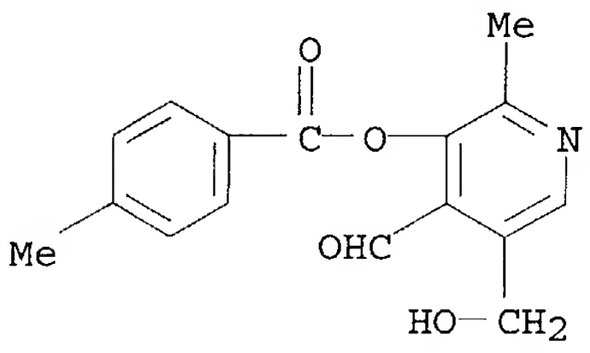
PAGE 2-A



RN 292611-37-1 USPATFULL
CN 2-Naphthalenecarboxylic acid, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)



RN 320591-83-1 USPATFULL
CN Benzoic acid, 4-methyl-, 4-formyl-5-(hydroxymethyl)-2-methyl-3-pyridinyl ester (9CI) (CA INDEX NAME)



L116 ANSWER 9 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2004:44997 USPATFULL
TITLE: Treatment of cardiovascular and related pathologies
INVENTOR(S): Sethi, Rajat, Winnipeg, CANADA
Haque, Wasimul, Edmonton, CANADA
PATENT ASSIGNEE(S): Medicure International Inc. (non-U.S. corporation)

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2004033990 | A1 | 20040219 |
| APPLICATION INFO.: | US 2003-639877 | A1 | 20030812 (10) |

RELATED APPLN. INFO.: Division of Ser. No. US 2000-645237, filed on 24 Aug 2000, PENDING

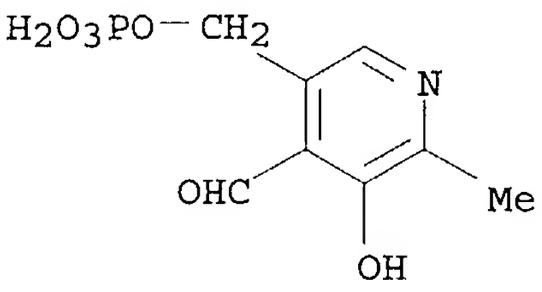
| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1999-150415P | 19990824 (60) |

DOCUMENT TYPE: Utility

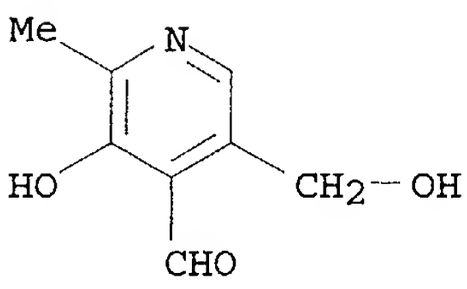
Searched by Barb O'Bryen, STIC 571-272-2518

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MERCHANT & GOULD PC, P.O. BOX 2903, MINNEAPOLIS, MN, 55402-0903
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 34 Drawing Page(s)
LINE COUNT: 1179
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for treating cardiovascular and related diseases such as myocardial infarction are described. The methods are directed to **concurrently** administering a compound such as pyridoxal-5'-phosphate, pyridoxamine, pyridoxal, or a 3-acylated pyridoxal analogue with a therapeutic cardiovascular compound.

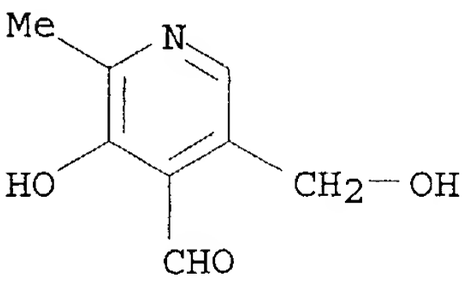
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **54-47-7**, Pyridoxal 5'-phosphate **66-72-8**, Pyridoxal **66-72-8D**, Pyridoxal, acylated analogs **85-87-0**, Pyridoxamine
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)
RN 54-47-7 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]- (9CI) (CA INDEX NAME)



RN 66-72-8 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-5-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)

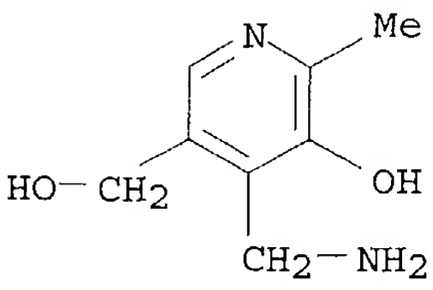


RN 66-72-8 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-5-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)

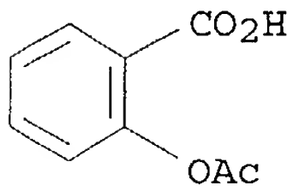


RN 85-87-0 USPATFULL
CN 3-Pyridinemethanol, 4-(aminomethyl)-5-hydroxy-6-methyl- (9CI) (CA INDEX NAME)

Searched by Barb O'Bryen, STIC 571-272-2518

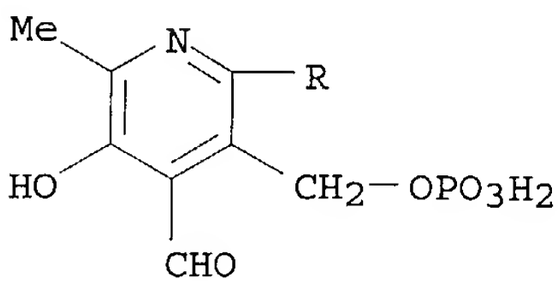


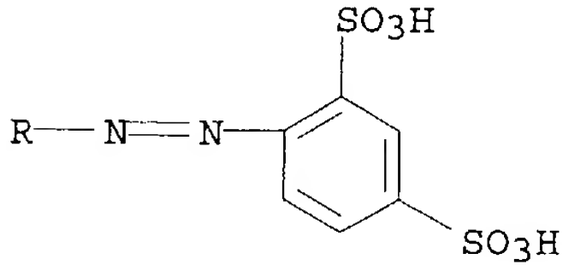
IT **50-78-2, Aspirin 9005-49-6, Heparin**
, biological studies **149017-66-3**
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)
RN 50-78-2 USPATFULL
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



RN 9005-49-6 USPATFULL
CN Heparin (8CI, 9CI) (CA INDEX NAME)

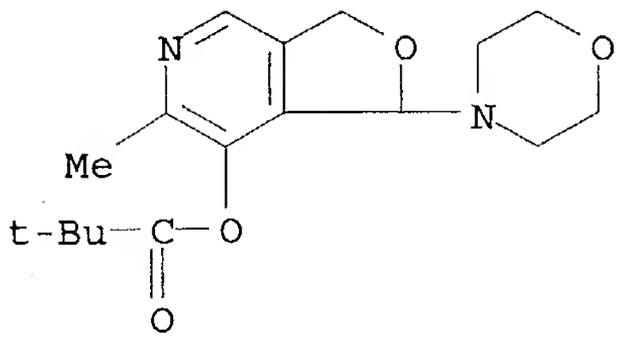
**STRUCTURE DIAGRAM IS NOT AVAILABLE**
RN 149017-66-3 USPATFULL
CN 1,3-Benzenedisulfonic acid, 4-[[4-formyl-5-hydroxy-6-methyl-3-[(phosphonooxy)methyl]-2-pyridinyl]azo]- (9CI) (CA INDEX NAME)



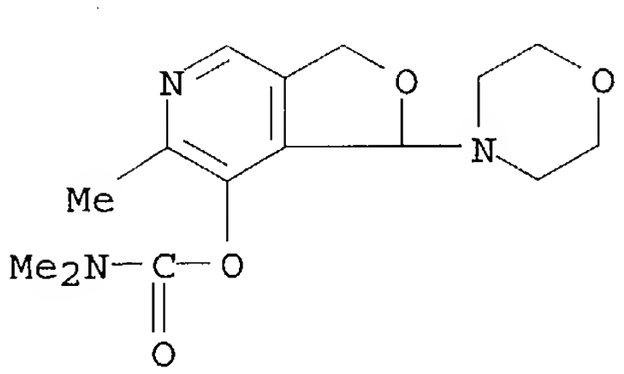


IT **292611-24-6P 292611-25-7P 292611-26-8P**
**292611-32-6P 292611-36-0P 292611-37-1P**
**320591-83-1P**
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)
RN 292611-24-6 USPATFULL
CN Propanoic acid, 2,2-dimethyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

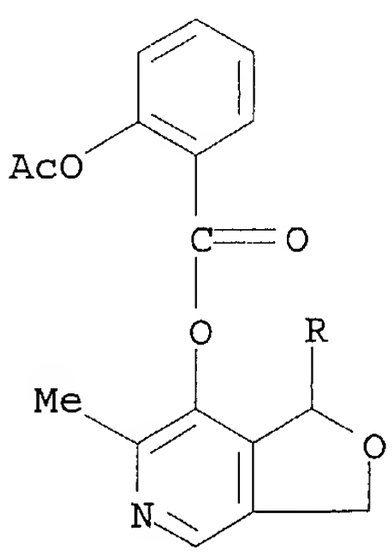
Searched by Barb O'Bryen, STIC 571-272-2518



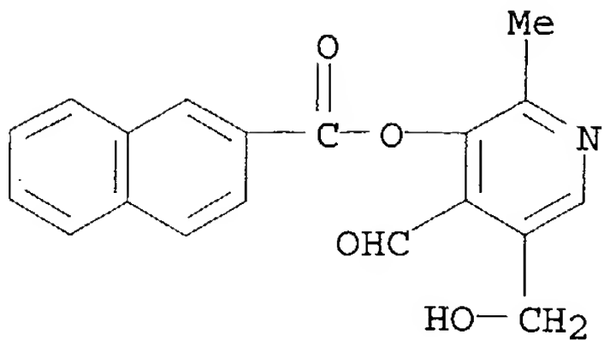
RN 292611-25-7 USPATFULL
CN Carbamic acid, dimethyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)



RN 292611-26-8 USPATFULL
CN Benzoic acid, 2-(acetyloxy)-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

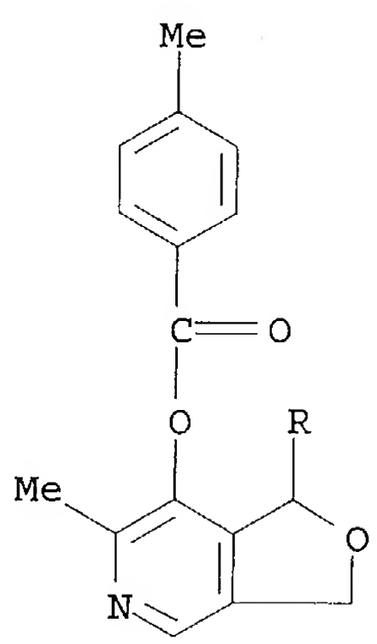


RN 292611-32-6 USPATFULL
CN 2-Naphthalenecarboxylic acid, 4-formyl-5-(hydroxymethyl)-2-methyl-3-pyridinyl ester (9CI) (CA INDEX NAME)

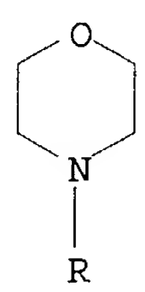


RN 292611-36-0 USPATFULL
CN Benzoic acid, 4-methyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

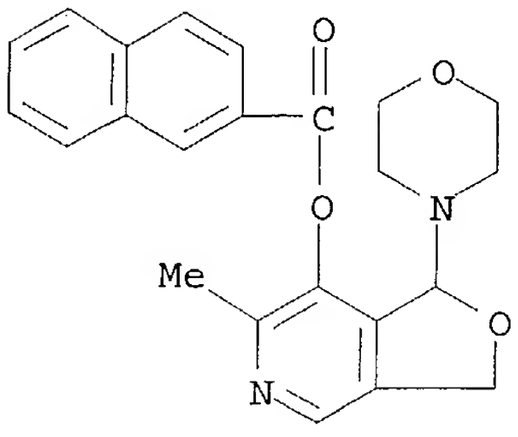
PAGE 1-A



PAGE 2-A

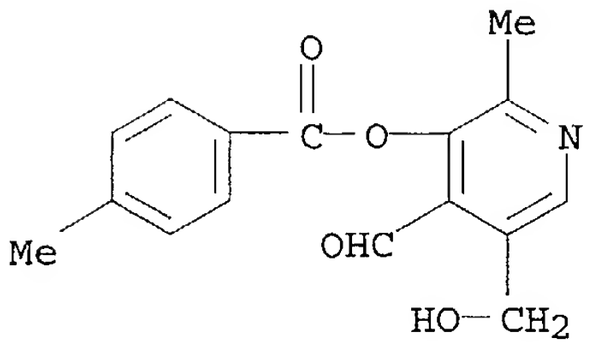


RN 292611-37-1 USPATFULL
CN 2-Naphthalenecarboxylic acid, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)



Searched by Barb O'Bryen, STIC 571-272-2518

RN 320591-83-1 USPATFULL
CN Benzoic acid, 4-methyl-, 4-formyl-5-(hydroxymethyl)-2-methyl-3-pyridinyl ester (9CI) (CA INDEX NAME)




L116 ANSWER 10 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2004:44996 USPATFULL
TITLE: Treatment of cardiovascular and related pathologies
INVENTOR(S): Sethi, Rajat, Winnipeg, CANADA
Haque, Wasimul, Edmonton, CANADA
PATENT ASSIGNEE(S): Medicure International Inc. (non-U.S. corporation)

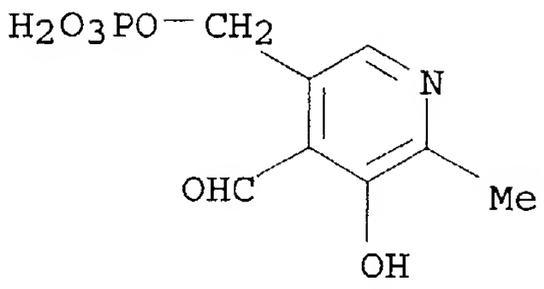
| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2004033989 | A1 | 20040219 |
| APPLICATION INFO.: | US 2003-639876 | A1 | 20030812 (10) |

RELATED APPLN. INFO.: Division of Ser. No. US 2000-645237, filed on 24 Aug 2000, PENDING

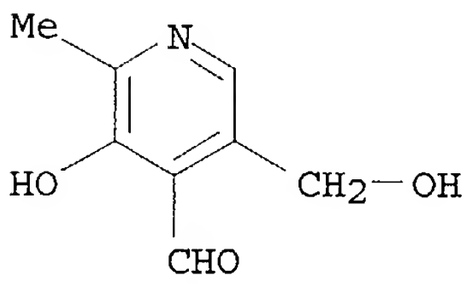
| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1999-150415P | 19990824 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MERCHANT & GOULD PC, P.O. BOX 2903, MINNEAPOLIS, MN, 55402-0903
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 34 Drawing Page(s)
LINE COUNT: 1169
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for treating cardiovascular and related diseases such as arrhythmia are described. The methods are directed to **concurrently** administering a compound such as pyridoxal-5'-phosphate, pyridoxamine, pyridoxal, or a 3-acylated pyridoxal analogue with a therapeutic cardiovascular compound.

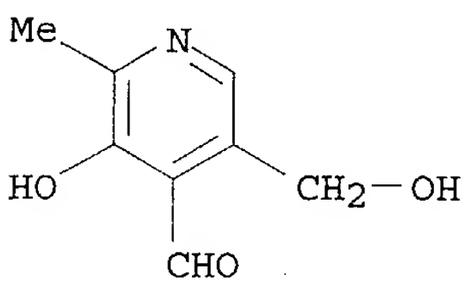
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **54-47-7**, Pyridoxal 5'-phosphate **66-72-8**, Pyridoxal **66-72-8D**, Pyridoxal, acylated analogs **85-87-0**, Pyridoxamine
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)
RN 54-47-7 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]- (9CI) (CA INDEX NAME)



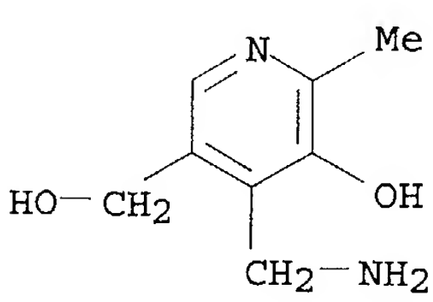
RN 66-72-8 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-5-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)



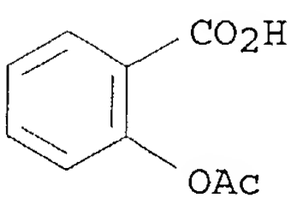
RN 66-72-8 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-5-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)



RN 85-87-0 USPATFULL
CN 3-Pyridinemethanol, 4-(aminomethyl)-5-hydroxy-6-methyl- (9CI) (CA INDEX NAME)



IT **50-78-2**, **Aspirin** **9005-49-6**, **Heparin**
, biological studies **149017-66-3**
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)
RN 50-78-2 USPATFULL
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)

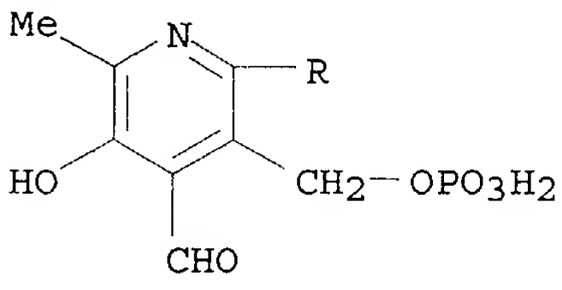


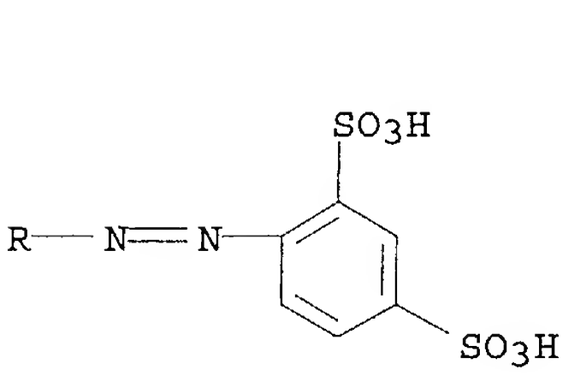
Searched by Barb O'Bryen, STIC 571-272-2518

RN 9005-49-6 USPATFULL
CN Heparin (8CI, 9CI) (CA INDEX NAME)

**STRUCTURE DIAGRAM IS NOT AVAILABLE**

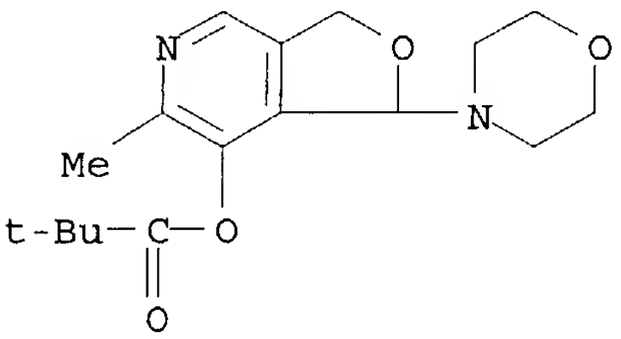
RN 149017-66-3 USPATFULL
CN 1,3-Benzenedisulfonic acid, 4-[[4-formyl-5-hydroxy-6-methyl-3-[(phosphonooxy)methyl]-2-pyridinyl]azo]- (9CI) (CA INDEX NAME)



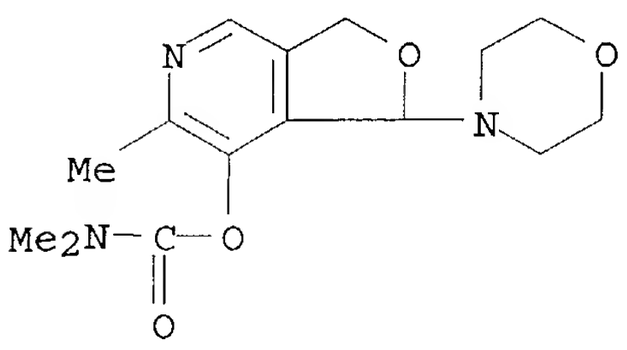




IT **292611-24-6P 292611-25-7P 292611-26-8P**
**292611-32-6P 292611-36-0P 292611-37-1P**
**320591-83-1P**
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)

RN 292611-24-6 USPATFULL
CN Propanoic acid, 2,2-dimethyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

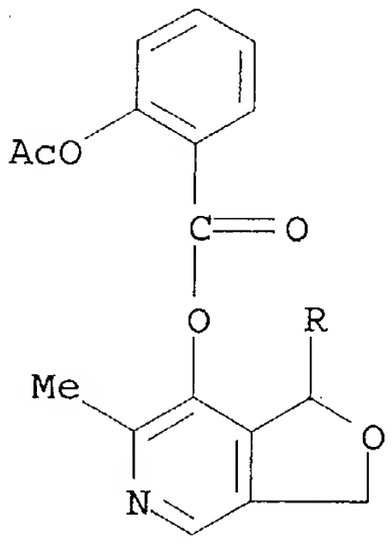


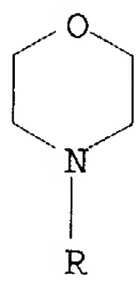

RN 292611-25-7 USPATFULL
CN Carbamic acid, dimethyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)



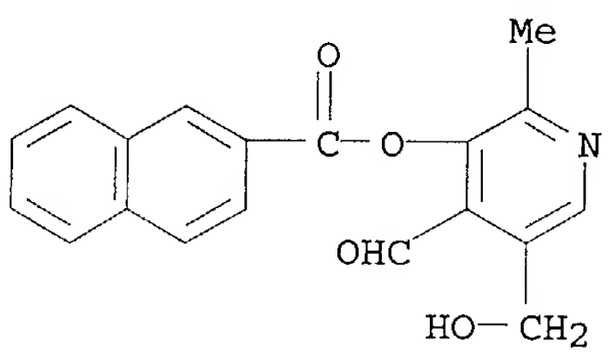

Searched by Barb O'Bryen, STIC 571-272-2518

RN 292611-26-8 USPATFULL
CN Benzoic acid, 2-(acetyloxy)-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)



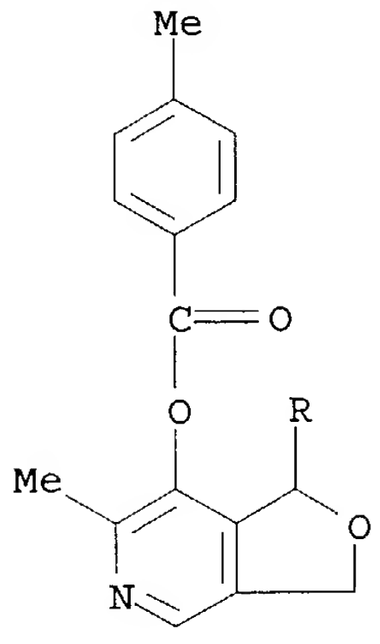

RN 292611-32-6 USPATFULL
CN 2-Naphthalenecarboxylic acid, 4-formyl-5-(hydroxymethyl)-2-methyl-3-pyridinyl ester (9CI) (CA INDEX NAME)



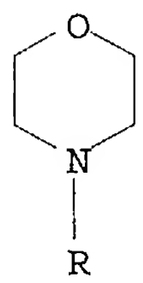

RN 292611-36-0 USPATFULL
CN Benzoic acid, 4-methyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

Searched by Barb O'Bryen, STIC 571-272-2518

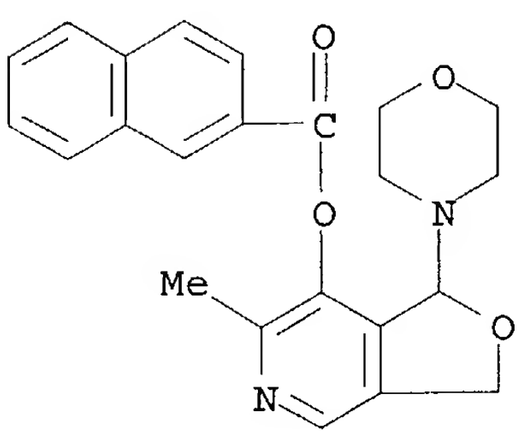
PAGE 1-A



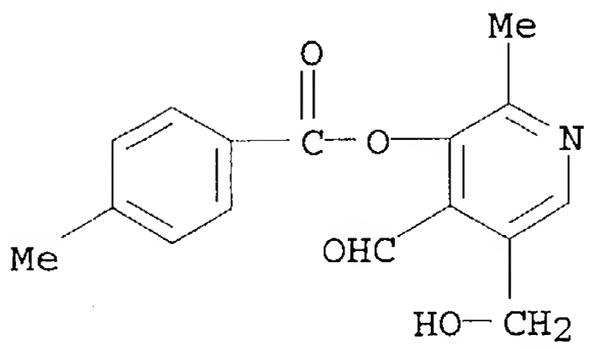
PAGE 2-A



RN 292611-37-1 USPATFULL
CN 2-Naphthalenecarboxylic acid, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)



RN 320591-83-1 USPATFULL
CN Benzoic acid, 4-methyl-, 4-formyl-5-(hydroxymethyl)-2-methyl-3-pyridinyl ester (9CI) (CA INDEX NAME)



Searched by Barb O'Bryen, STIC 571-272-2518

L116 ANSWER 11 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2004:9618 USPATFULL
TITLE: Treatment of cardiovascular and related pathologies
INVENTOR(S): Sethi, Rajat, Winnipeg, CANADA
Haque, Wasimul, Edmonton, CANADA
PATENT ASSIGNEE(S): Medicure International Inc., Barbados, CAYMAN ISLANDS (non-U.S. corporation)

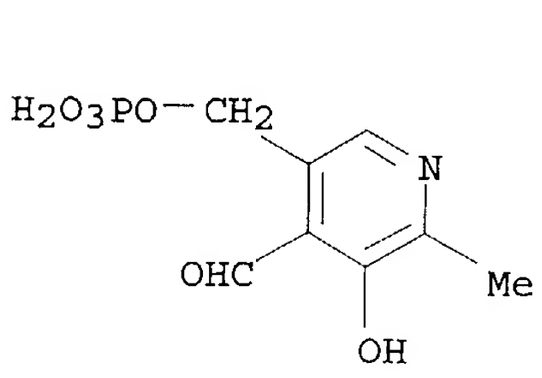
| | NUMBER | KIND | DATE | |
|---|---|---|---|---|
| PATENT INFORMATION: | US 6677356 | B1 | 20040113 | |
| APPLICATION INFO.: | US 2000-645237 | | 20000824 | (9) |

| | NUMBER | DATE | |
|---|---|---|---|
| PRIORITY INFORMATION: | US 1999-150415P | 19990824 | (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Jones, Dwayne C.
LEGAL REPRESENTATIVE: Merchant & Gould P.C.
NUMBER OF CLAIMS: 36
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 34 Drawing Figure(s); 34 Drawing Page(s)
LINE COUNT: 1398
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

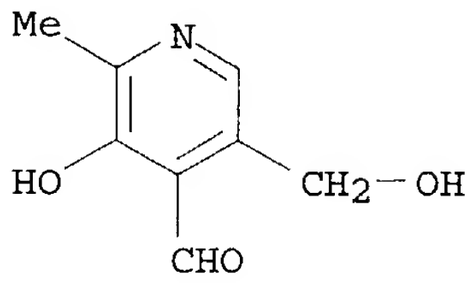
AB Methods for treating cardiovascular and related diseases such as hypertrophy, hypertension, congestive heart failure, ischemia, ischemia reperfusion injuries in various organs, arrhythmia, and myocardial infarction, are described. The methods are directed to **concurrently** administering a compound such as pyridoxal-5'-phosphate, pyridoxamine, pyridoxal, or a 3-acylated pyridoxal analogue with a therapeutic cardiovascular compound.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **54-47-7**, Pyridoxal 5'-phosphate **66-72-8**, Pyridoxal **66-72-8D**, Pyridoxal, acylated analogs **85-87-0**, Pyridoxamine
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)
RN 54-47-7 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]- (9CI) (CA INDEX NAME)

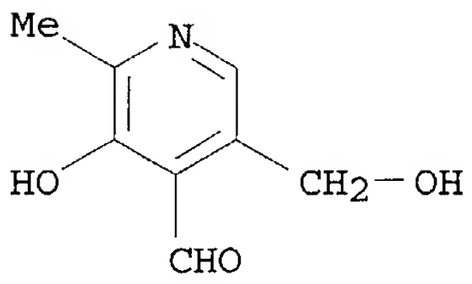



RN 66-72-8 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-5-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)

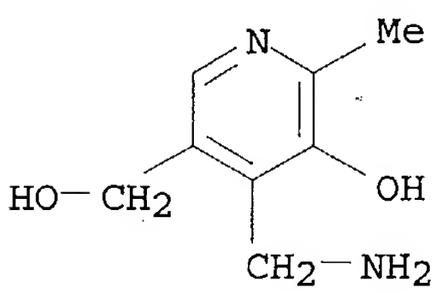
Searched by Barb O'Bryen, STIC 571-272-2518



RN 66-72-8 USPATFULL
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-5-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)

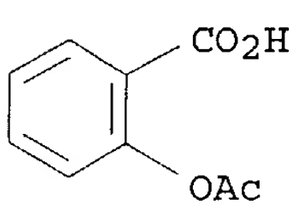


RN 85-87-0 USPATFULL
CN 3-Pyridinemethanol, 4-(aminomethyl)-5-hydroxy-6-methyl- (9CI) (CA INDEX NAME)



IT **50-78-2, Aspirin 9005-49-6, Heparin**
, biological studies **149017-66-3**
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)

RN 50-78-2 USPATFULL
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)

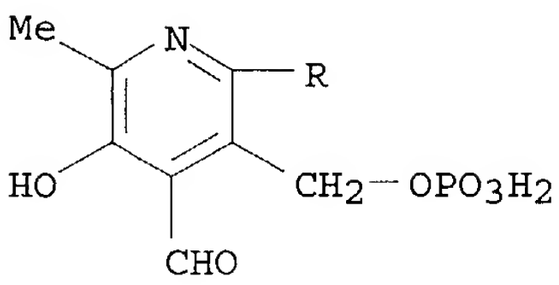


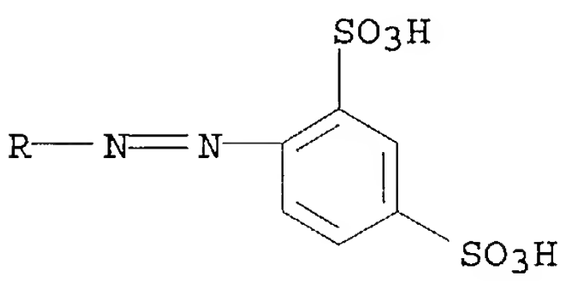
RN 9005-49-6 USPATFULL
CN Heparin (8CI, 9CI) (CA INDEX NAME)

**STRUCTURE DIAGRAM IS NOT AVAILABLE**

RN 149017-66-3 USPATFULL
CN 1,3-Benzenedisulfonic acid, 4-[[4-formyl-5-hydroxy-6-methyl-3-[(phosphonooxy)methyl]-2-pyridinyl]azo]- (9CI) (CA INDEX NAME)

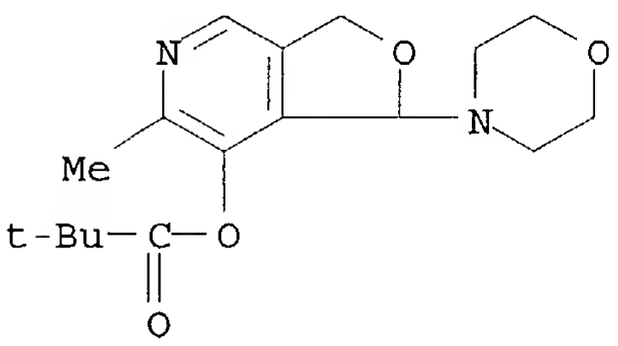
Searched by Barb O'Bryen, STIC 571-272-2518



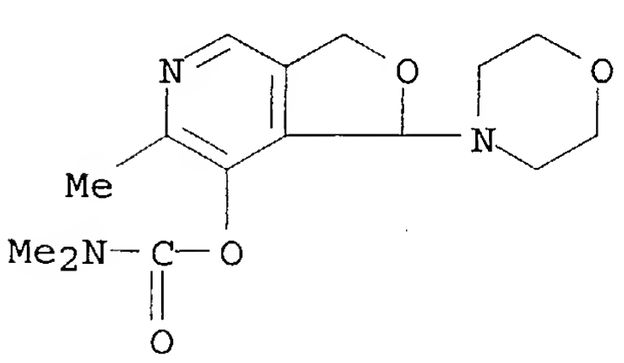


IT **292611-24-6P 292611-25-7P 292611-26-8P**
**292611-32-6P 292611-36-0P 292611-37-1P**
**320591-83-1P**
(treatment of cardiovascular and related pathologies with pyridoxal derivs.)

RN 292611-24-6 USPATFULL
CN Propanoic acid, 2,2-dimethyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

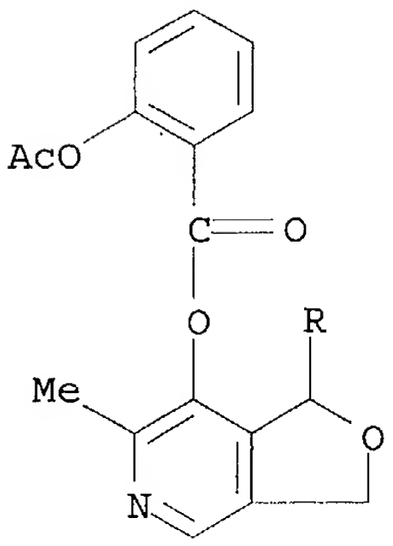


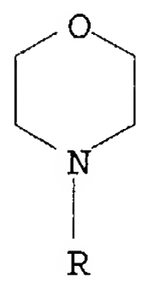
RN 292611-25-7 USPATFULL
CN Carbamic acid, dimethyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)



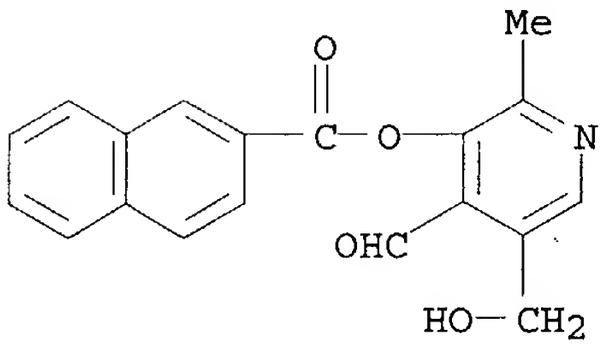
RN 292611-26-8 USPATFULL
CN Benzoic acid, 2-(acetyloxy)-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

Searched by Barb O'Bryen, STIC 571-272-2518



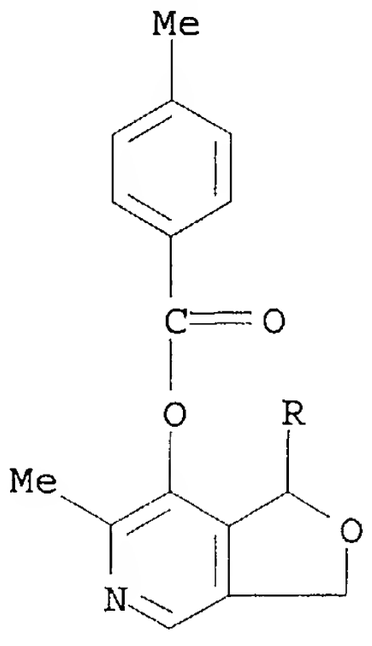


RN 292611-32-6 USPATFULL
CN 2-Naphthalenecarboxylic acid, 4-formyl-5-(hydroxymethyl)-2-methyl-3-pyridinyl ester (9CI) (CA INDEX NAME)



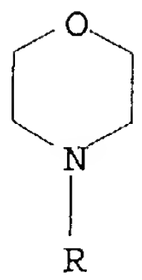
RN 292611-36-0 USPATFULL
CN Benzoic acid, 4-methyl-, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)

PAGE 1-A

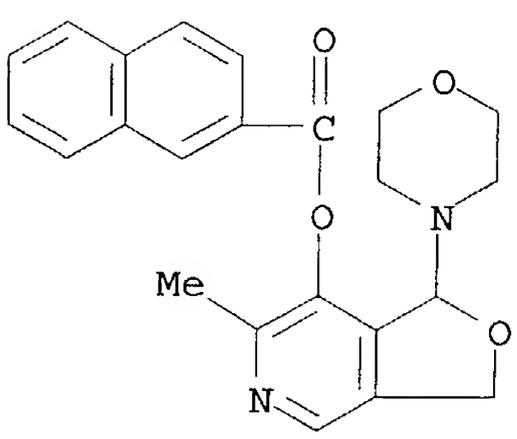


Searched by Barb O'Bryen, STIC 571-272-2518

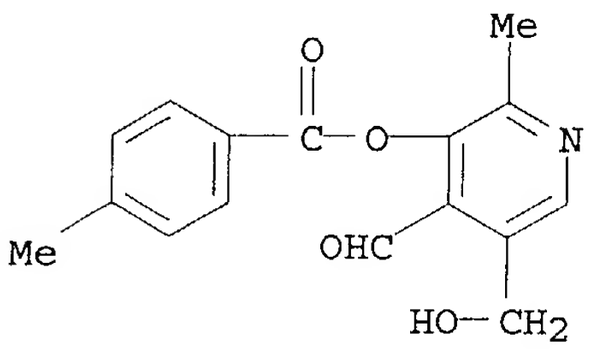
PAGE 2-A



RN 292611-37-1 USPATFULL
CN 2-Naphthalenecarboxylic acid, 1,3-dihydro-6-methyl-1-(4-morpholinyl)furo[3,4-c]pyridin-7-yl ester (9CI) (CA INDEX NAME)



RN 320591-83-1 USPATFULL
CN Benzoic acid, 4-methyl-, 4-formyl-5-(hydroxymethyl)-2-methyl-3-pyridinyl ester (9CI) (CA INDEX NAME)



L116 ANSWER 12 OF 27 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 85238958 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2409394
TITLE: Prevention of thrombosis in arteries: novel approaches.
AUTHOR: Verstraete M
SOURCE: Journal of cardiovascular pharmacology, (1985) 7 Suppl 3 S191-205. Ref: 135
Journal code: 7902492. ISSN: 0160-2446.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198507
ENTRY DATE: Entered STN: 19900320

Searched by Barb O'Bryen, STIC 571-272-2518

Last Updated on STN: 20000303
Entered Medline: 19850730

ABSTRACT:
A number of drugs such as unfractionated heparin, oral anticoagulants, and agents inhibiting platelet function, are being used in the prevention of arterial thrombosis; novel antithrombotic substances are in the making. Among the latter are low-mol-wt heparin and semisynthetic heparin analogs, unfractionated and low-mol-wt heparin covalently complexed or not with anti-thrombin III, pyridoxal phosphate, scavengers of free radicals, synthetic inhibitors of serine proteases, and stimulators of endogenous fibrinolysis.

CONTROLLED TERM: Check Tags: Human
Anticoagulants: PD, pharmacology
Blood Coagulation Factors: BI, biosynthesis
Blood Proteins: ME, metabolism
Fibrinolysis: DE, drug effects
Free Radicals
**Heparin: AA, analogs & derivatives**
**Heparin: ME, metabolism**
**Heparin: TU, therapeutic use**
Lipid Peroxides: ME, metabolism
**Platelet Adhesiveness: DE, drug effects**
**Platelet Aggregation: DE, drug effects**
Platelet-Derived Growth Factor: AI, antagonists & inhibitors
Protease Inhibitors
Prothrombin Time
**Pyridoxal Phosphate: PD, pharmacology**
Serine Endopeptidases
***Thrombosis: PC, prevention & control**
Vitamin E: PD, pharmacology
Vitamin K: PD, pharmacology

CAS REGISTRY NO.: 12001-79-5 (Vitamin K); 1406-18-4 (Vitamin E); 54-47-7 (Pyridoxal Phosphate); 9005-49-6 (Heparin)

CHEMICAL NAME: 0 (Anticoagulants); 0 (Blood Coagulation Factors); 0 (Blood Proteins); 0 (Free Radicals); 0 (Lipid Peroxides); 0 (Platelet-Derived Growth Factor); 0 (Protease Inhibitors); EC 3.4.21 (Serine Endopeptidases)

L116 ANSWER 13 OF 27 MEDLINE on STN
ACCESSION NUMBER: 92119060 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1768765
TITLE: Effect of phosphopyridoxylation on thrombin interaction with platelet glycoprotein Ib.
AUTHOR: Ternisien C; Jandrot-Perrus M; Huisse M G; Guillin M C
CORPORATE SOURCE: Laboratoire de Recherche sur l'Hemostase et la Thrombose, Faculte Xavier Bichat, Paris, France.
SOURCE: Blood coagulation & fibrinolysis : an international journal in haemostasis and thrombosis, (1991 Aug) 2 (4) 521-8. Journal code: 9102551. ISSN: 0957-5235.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199202
ENTRY DATE: Entered STN: 19920315
Last Updated on STN: 19920315
Entered Medline: 19920227

ABSTRACT:
The purpose of this study was to determine the effect of chemical modification of lysyl residues on thrombin interaction with platelet membrane proteins. Modification of lysyl residues by pyridoxal-5'-phosphate affected two different sites on thrombin and resulted in a greatly decreased binding to platelets.

Using a crosslinking bifunctional reagent [bis(sulphosuccinimidyl) suberate (BS3)], we show that modified thrombin retained the ability to form high molecular mass (greater than or equal to 400 kDa) complexes with yet unidentified platelet proteins and to bind to platelet protease nexin I, but had lost the ability to bind to platelet glycoprotein Ib (GPIb). As previously reported by others, heparin protected one of the two sites from phosphopyridoxylation. In contrast modified thrombin, heparin-protected modified thrombin retained the ability to bind to GPIb, indicating that the lysyl residue(s) protected by heparin from the modification are essential for GPIb binding. While unprotected modified thrombin failed to bind hirudin, heparin-protected modified thrombin retained its ability to bind the carboxy-terminal hirudin peptide H54-65. Tritium-labelling of the modified lysyl residues and degradation of modified thrombins by CNBr or trypsin confirmed that the lysyl residue(s) protected by heparin and essential for GPIb binding are located in the thrombin binding domain for the carboxyl-terminal tail of hirudin, within the sequence 18-73 of the thrombin B chain.

CONTROLLED TERM: Check Tags: Human; Support, Non-U.S. Gov't
Binding Sites
Cross-Linking Reagents
Cyanogen Bromide
**Heparin: PD, pharmacology**
**Hirudin: ME, metabolism**
Lysine: ME, metabolism
Molecular Weight
**Platelet Aggregation: DE, drug effects**
*Platelet Membrane Glycoproteins: ME, metabolism
Protein Binding
***Pyridoxal Phosphate: ME, metabolism**
*Thrombin: ME, metabolism
Thrombin: PD, pharmacology
Tritium
Trypsin

CAS REGISTRY NO.: 10028-17-8 (Tritium); 506-68-3 (Cyanogen Bromide); 54-47-7 (Pyridoxal Phosphate); 56-87-1 (Lysine); 8001-27-2 (Hirudin); 9005-49-6 (Heparin)

CHEMICAL NAME: 0 (Cross-Linking Reagents); 0 (Platelet Membrane Glycoproteins); EC 3.4.21.4 (Trypsin); EC 3.4.21.5 (Thrombin)

L116 ANSWER 14 OF 27 MEDLINE on STN
ACCESSION NUMBER: 84203959 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6202339
TITLE: [Inhibition of platelet aggregation and cyclic nucleotide phosphodiesterase (specifically cyclAMP) by 3-hydroxypyridine derivatives].
Tormozhenie agregatsii i ingibirovanie fosfodiesterazy tsiklicheskikh nukleotidov (spetsifichnoi dlia tsAMF) trombotsitov proizvodnymi 3-oksipiridina.
AUTHOR: Kagan V E; Polianskii N B; Muranov K O; Shvedova A A; Smirnov L D
SOURCE: Biulleten' eksperimental'noi biologii i meditsiny, (1984 Apr) 97 (4) 416-8.
Journal code: 0370627. ISSN: 0365-9615.
PUB. COUNTRY: USSR
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198407
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19900319
Entered Medline: 19840713

ABSTRACT:

Searched by Barb O'Bryen, STIC 571-272-2518

The effects of 3-hydroxypyridine (3-HP) derivatives on platelet aggregation and platelet phosphodiesterase (PDE) of cyclic nucleotides (cAMP-dependent) were studied. It was shown that some derivatives of 3-HP inhibit platelet aggregation (the most pronounced effect was exerted by 2-benzyl-3- oxypyridine ). Several derivatives o 3-HP given in a concentration 10(-3) M were discovered to inhibit PDE by 40 to 75%. No correlation was found between the efficacy of 3-HP as antiaggregation agents and PDE inhibitors.

CONTROLLED TERM: Check Tags: Human
1-Methyl-3-isobutylxanthine: PD, pharmacology
*3',5'-Cyclic-Nucleotide Phosphodiesterase: AI, antagonists & inhibitors
**Aspirin: PD, pharmacology**
English Abstract
***Platelet Aggregation: DE, drug effects**
*Pyridines: PD, pharmacology
**Pyridoxal: PD, pharmacology**
**Pyridoxal Phosphate: PD, pharmacology**
Theophylline: PD, pharmacology

CAS REGISTRY NO.: 109-00-2 (3-hydroxypyridine); 28822-58-4 (1-Methyl-3-isobutylxanthine); 50-78-2 (Aspirin); 54-47-7 (Pyridoxal Phosphate); 58-55-9 (Theophylline); 66-72-8 (Pyridoxal)

CHEMICAL NAME: 0 (Pyridines); EC 3.1.4.17 (3',5'-Cyclic-Nucleotide Phosphodiesterase)

L116 ANSWER 15 OF 27 MEDLINE on STN
ACCESSION NUMBER: 81117260 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6780552
TITLE: Structure-function relations in platelet-thrombin reactions. Inhibition of platelet-thrombin interactions by lysine modification.
AUTHOR: White G C; Lundblad R L; Griffith M J
CONTRACT NUMBER: DE 02668 (NIDCR)
RR-4433 (NCRR)
RR-46-20S1 (NCRR)
SOURCE: Journal of biological chemistry, (1981 Feb 25) 256 (4) 1763-6.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198104
ENTRY DATE: Entered STN: 19900316
Last Updated on STN: 20000303
Entered Medline: 19810421

ABSTRACT:
The chemical modification of lysine residues in human alpha-thrombin has been used to study the interaction of thrombin with human platelets. Phosphopyridoxylation of thrombin using pyridoxal 5'-phosphate (pyridoxal-P) has been shown to inhibit the fibrinogen clotting activity of thrombin but not the catalytic activity (Griffith, M. J. J. Biol. Chem. 254, 3401-3406). Phosphopyridoxylation resulted in marked inhibition of the platelet-activating activity of thrombin. The concentration of pyridoxal-P-thrombin required to induce half-maximal platelet aggregation and release was 60 times greater than that of unmodified thrombin. Binding studies using pyridoxal-P-125I-thrombin showed a loss of both high and low affinity binding of thrombin to the surface of intact gel filtered platelets. In contrast, thrombin modified with pyridoxal-P in the presence of heparin incorporated up to 1 mol of pyridoxal-P per mol of thrombin. The heparin-protected pyridoxal-P-thrombin was only slightly inhibited in its interaction with platelets, and binding studies with the heparin-protected pyridoxal-P-125I-thrombin showed selective loss of low

affinity binding but preservation of high affinity binding. These results provide further support for the hypothesis that residues at the macromolecular binding site of thrombin are involved in the binding of thrombin to platelets and further separate this functional region of thrombin into two lysine-containing subregions, one which is protected from modification by heparin which is involved in high affinity binding, and another which is not protected by heparin which is involved in low affinity binding.

CONTROLLED TERM: Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Blood Platelets: DE, drug effects
*Blood Platelets: ME, metabolism
**Heparin: PD, pharmacology**
Kinetics
*Lysine
**Platelet Aggregation: DE, drug effects**
***Pyridoxal Phosphate: PD, pharmacology**
*Thrombin: ME, metabolism

CAS REGISTRY NO.: 54-47-7 (Pyridoxal Phosphate); 56-87-1 (Lysine); 9005-49-6 (Heparin)

CHEMICAL NAME: EC 3.4.21.5 (Thrombin)

L116 ANSWER 16 OF 27 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2004170519 EMBASE

TITLE: Pharmacological approach to diabetic retinopathy.

AUTHOR: De La Cruz M.D.J.P.; Gonzalez-Correa M.D.J.A.; Guerrero M.D.A.; Sanchez de la Cuesta M.D.F.

CORPORATE SOURCE: M.D.J.P. De La Cruz, Dept. of Pharmacology/Therapeutics, School of Medicine, University of Malaga, Campus de Teatinos s/n, E-29071 Malaga, Spain. jpcruz@uma.es

SOURCE: Diabetes/Metabolism Research and Reviews, (2004) 20/2 (91-113).
Refs: 246
ISSN: 1520-7552 CODEN: DMRRFM

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
012 Ophthalmology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:
Diabetic retinopathy is the most frequent cause of legal blindness in the population of 30-to-70-year olds. Whether retinopathy appears or not depends mainly on the duration of the disease and the degree of metabolic control the patient maintains. High blood glucose values lead to important changes in cellular metabolism and the main effects of these alterations are endothelial dysfunction that sets in motion the morphological process of diabetic retinopathy. The biochemical lesions caused by prolonged hyperglycemia can be positively influenced, but usually not normalized, pharmacologically with some groups of drugs, which are now under development. This makes tight control of glycemia a key measure in preventing the onset or progression of diabetic retinopathy, together with an effective program of ophthalmologic detection and follow-up in patients with diabetes. Regarding the role of endothelial dysfunction, antiplatelet drugs have been shown to slow some aspects of the evolution of diabetic retinopathy in its initial stages, mainly a lower degree of microaneurysms. However, a new approach to controlling endothelial dysfunction shows promise, mainly through the vascular endothelial growth factor (VEGF) inhibitors. These agents may prove to be especially useful in the

treatment of proliferative diabetic retinopathy. Other encouraging results have been obtained in studies of antioxidant drugs and inhibitors of the formation of advanced glycation end products. Once retinal lesions appear, preventive measures need to be redoubled, with special attention to controlling glycemia; however, it is also necessary to resort to laser photocoagulation. This intervention aims to eliminate areas of ischemia and to diminish the formation of retinal exudates. If this measure fails or if vitreous hemorrhage appears, the only remaining therapeutic measure is vitrectomy. Copyright .COPYRGT. 2004 John Wiley and Sons, Ltd.

CONTROLLED TERM: Medical Descriptors:
*diabetic retinopathy: CO, complication
*diabetic retinopathy: DI, diagnosis
*diabetic retinopathy: DT, drug therapy
*diabetic retinopathy: ET, etiology
*diabetic retinopathy: PC, prevention
*diabetic retinopathy: SU, surgery
blindness
population research
disease duration
metabolic regulation
glucose blood level
cell metabolism
endothelium
morphology
biochemistry
hyperglycemia: DT, drug therapy
disease course
ophthalmology
follow up
diabetes mellitus
microaneurysm: CO, complication
microaneurysm: DT, drug therapy
retina injury: PC, prevention
retina injury: SU, surgery
diabetes control
laser coagulation
retina ischemia: SU, surgery
retina exudate
vitreous hemorrhage: SU, surgery
vitrectomy
prevalence
oxidative stress
**thrombosis**
blood flow
retina blood vessel
drug efficacy
drug tolerability
liver necrosis: SI, side effect
enzyme inhibition
drug potency
human
nonhuman
clinical trial
review
priority journal
Drug Descriptors:
glucose: EC, endogenous compound
**antithrombocytic agent: CT, clinical trial**
**antithrombocytic agent: DT, drug therapy**
**antithrombocytic agent: PD, pharmacology**
vasculotropin: EC, endogenous compound

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vasculotropin inhibitor: DT, drug therapy
antioxidant: CB, drug combination
antioxidant: DT, drug therapy
antioxidant: PD, pharmacology
advanced glycation end product: EC, endogenous compound
polyol: EC, endogenous compound
diacylglycerol: EC, endogenous compound
protein kinase C: EC, endogenous compound
inducible nitric oxide synthase: EC, endogenous compound
hemoglobin A1c: EC, endogenous compound
glucagon: PD, pharmacology
sorbinil: AE, adverse drug reaction
sorbinil: CT, clinical trial
sorbinil: DT, drug therapy
sorbinil: PD, pharmacology
tolrestat: DT, drug therapy
tolrestat: PD, pharmacology
epalrestat: DT, drug therapy
epalrestat: PD, pharmacology
fidarestat: DT, drug therapy
fidarestat: PD, pharmacology
ruboxistaurin: DT, drug therapy
ruboxistaurin: PD, pharmacology
staurosporine: AE, adverse drug reaction
staurosporine: CM, drug comparison
staurosporine: DT, drug therapy
staurosporine: PD, pharmacology
1 (5 isoquinolinesulfonyl) 2 methylpiperazine: AE, adverse drug reaction
1 (5 isoquinolinesulfonyl) 2 methylpiperazine: CM, drug comparison
1 (5 isoquinolinesulfonyl) 2 methylpiperazine: DT, drug therapy
1 (5 isoquinolinesulfonyl) 2 methylpiperazine: PD, pharmacology
2 [1 (3 dimethylaminopropyl) 3 indolyl] 3 (3 indolyl)maleimide: AE, adverse drug reaction
2 [1 (3 dimethylaminopropyl) 3 indolyl] 3 (3 indolyl)maleimide: CM, drug comparison
2 [1 (3 dimethylaminopropyl) 3 indolyl] 3 (3 indolyl)maleimide: DT, drug therapy
2 [1 (3 dimethylaminopropyl) 3 indolyl] 3 (3 indolyl)maleimide: PD, pharmacology
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: PD, pharmacology
aminoguanidine: CT, clinical trial
aminoguanidine: DT, drug therapy
aminoguanidine: PD, pharmacology
alpha tocopherol: CB, drug combination
alpha tocopherol: DT, drug therapy
alpha tocopherol: PD, pharmacology
hydrazine derivative: DT, drug therapy
hydrazine derivative: PD, pharmacology
pyridoxine derivative: DT, drug therapy
pyridoxine derivative: PD, pharmacology
**pyridoxamine: DT, drug therapy**
**pyridoxamine: PD, pharmacology**
glutathione: CB, drug combination
glutathione: DT, drug therapy
glutathione: PD, pharmacology
ascorbic acid: CB, drug combination
ascorbic acid: DT, drug therapy

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ascorbic acid: PD, pharmacology
acetylcysteine: CB, drug combination
acetylcysteine: DT, drug therapy
acetylcysteine: PD, pharmacology
unindexed drug

CAS REGISTRY NO.: (glucose) 50-99-7, 84778-64-3; (vasculotropin) 127464-60-2; (protein kinase C) 141436-78-4; (inducible nitric oxide synthase) 501433-35-8; (hemoglobin A1c) 62572-11-6; (glucagon) 11140-85-5, 62340-29-8, 9007-92-5; (sorbinil) 68367-52-2; (tolrestat) 82964-04-3; (epalrestat) 82159-09-9; (fidarestat) 105300-43-4; (ruboxistaurin) 169939-93-9, 169939-94-0; (staurosporine) 62996-74-1; (1 (5 isoquinolinesulfonyl) 2 methylpiperazine) 84477-87-2; (2 [1 (3 dimethylaminopropyl) 3 indolyl] 3 (3 indolyl)maleimide) 133052-90-1; (aminoguanidine) 1068-42-4, 2582-30-1, 79-17-4; (alpha tocopherol) 1406-18-4, 1406-70-8, 52225-20-4, 58-95-7, 59-02-9; (pyridoxamine) 13876-70-5, 5103-96-8, 524-36-7, **85-87-0**; (glutathione) 70-18-8; (ascorbic acid) 134-03-2, 15421-15-5, 50-81-7; (acetylcysteine) 616-91-1

CHEMICAL NAME: Ly 333531; H 7; Gf 109203x

L116 ANSWER 17 OF 27 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
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ACCESSION NUMBER: 2002432506 EMBASE
TITLE: EDTA chelation therapy for atherosclerosis and degenerative diseases: Implausibility and paradoxical oxidant effects.
AUTHOR: Green S.; Sampson W.
CORPORATE SOURCE: Prof. Dr. W. Sampson, 841 Santa Rita Avenue, Los Altos, CA 94022, United States. wisampson@cs.com
SOURCE: Scientific Review of Alternative Medicine, (2002) 6/1 (17-22).
Refs: 39
ISSN: 1095-0656 CODEN: SRAMFK
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
036 Health Policy, Economics and Management
030 Pharmacology
038 Adverse Reactions Titles
037 Drug Literature Index
017 Public Health, Social Medicine and Epidemiology
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT:
Planned clinical trials of ethylene-diamine-tetra-acetic acid (EDTA) chelation therapy by the National Center for Complementary and Alternative Medicine and others call for investigation of chelation's biochemistry and pharmacology, its toxicity, and the history of claims made for it. EDTA, known to reduce serum levels of polyvalent metals by chelation, was proposed in the late 1950s for removal of calcium from atherosclerotic plaques. Proponents now claim that EDTA can remove toxic heavy-metal ions and that it can neutralize or reduce oxygen free radicals. A review of atherosclerosis pathophysiology and EDTA chemistry reveals that (1) EDTA chelation effectiveness is implausible; (2) the preponderance of evidence shows ineffectiveness; and (3) EDTA augments oxidative reactions involving iron instead of inhibiting them, resulting in increased likelihood of production of oxygen free radicals rather than neutralization of them, as claimed. Further investigation of this therapy for atherosclerosis and degenerative diseases may be ethically questioned.

CONTROLLED TERM: Medical Descriptors:
*degenerative disease: TH, therapy

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*degenerative disease: DM, disease management
*degenerative disease: DT, drug therapy
*atherosclerosis: TH, therapy
*atherosclerosis: DM, disease management
*atherosclerosis: DT, drug therapy
*chelation therapy
human
clinical trial
nonhuman
pathophysiology
atherosclerotic plaque
chemistry
aerobic metabolism
medical ethics
quantitative analysis
clinical protocol
pathology
health care cost
calcium metabolism
medicolegal aspect
supplementation
drug excretion
hypocalcemia: SI, side effect
tetany: SI, side effect
heart muscle contractile force
side effect: SI, side effect
heart arrhythmia: SI, side effect
in vitro study
kidney tubule necrosis: SI, side effect
hypotension: SI, side effect
bone marrow depression: SI, side effect
drug hypersensitivity: SI, side effect
review
Drug Descriptors:
*edetic acid: DT, drug therapy
*edetic acid: CT, clinical trial
*edetic acid: PD, pharmacology
*edetic acid: IV, intravenous drug administration
*edetic acid: CB, drug combination
*edetic acid: PK, pharmacokinetics
*edetic acid: AE, adverse drug reaction
metal
calcium: DT, drug therapy
calcium: CB, drug combination
metal ion
heavy metal
free radical
iron
reducing agent
heparin: DT, drug therapy
**heparin: CB, drug combination**
magnesium chloride: DT, drug therapy
magnesium chloride: CB, drug combination
lidocaine: DT, drug therapy
lidocaine: CB, drug combination
pyridoxamine: DT, drug therapy
**pyridoxamine: CB, drug combination**
vitamin B complex: DT, drug therapy
vitamin B complex: CB, drug combination
ascorbic acid: DT, drug therapy
ascorbic acid: CB, drug combination
ascorbic acid: PO, oral drug administration

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alpha tocopherol
magnesium
copper

CAS REGISTRY NO.: (edetic acid) 150-43-6, 60-00-4; (calcium) 7440-70-2; (iron) 14093-02-8, 53858-86-9, 7439-89-6; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (magnesium chloride) 7786-30-3, 7791-18-6; (lidocaine) 137-58-6, 24847-67-4, 56934-02-2, 73-78-9; (pyridoxamine) 13876-70-5, 5103-96-8, 524-36-7, 85-87-0; (ascorbic acid) 134-03-2, 15421-15-5, 50-81-7; (alpha tocopherol) 1406-18-4, 1406-70-8, 52225-20-4, 58-95-7, 59-02-9; (magnesium) 7439-95-4; (copper) 15158-11-9, 7440-50-8

L116 ANSWER 18 OF 27 TOXCENTER COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:14389 TOXCENTER
DOCUMENT NUMBER: PubMed ID: 11133615
TITLE: The anesthetic interaction between adenosine triphosphate and N-methyl-D-aspartate receptor antagonists in the rat
AUTHOR(S): Masaki E; Yamazaki K; Ohno Y; Nishi H; Matsumoto Y; Kawamura M
CORPORATE SOURCE: Department of Pharmacology (I), Jikei University School of Medicine, Tokyo 105-8461, Japan. jkyakuri@sepia.ocn.ne.jp
SOURCE: Anesthesia and analgesia, (2001 Jan) 92 (1) 134-9. Journal Code: 1310650. ISSN: 0003-2999.
COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDLINE
OTHER SOURCE: MEDLINE 2001087706
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20011116

ABSTRACT:
Modulation of synaptic neurotransmission through the ligand-gated ion channel is probably involved in the mechanisms of analgesic and anesthetic actions. In the central nervous system, adenosine triphosphate and glutamate are fast excitatory neurotransmitters through their effects on P2X and N-methyl-D-aspartate (NMDA) receptors respectively. To examine the anesthetic interaction between adenosine triphosphate and NMDA receptor antagonists, we studied the effect of intracerebroventricular administration of P2 and/or NMDA antagonists on the minimum alveolar concentration (MAC) of sevoflurane in rats. Intracerebro- ventricular administration of phosphonopentanoic acid azophenyl-2',4'-disulfonate and D (-)-2-anino-5-phophonopentanoic acid, P2 and NMDA antagonists, significantly reduced the MAC of sevoflurane. The reduction of the MAC by both phosphonopentanoic acid azophenyl-2',4'-disulfonate and D (-)-2-anino-5-phophonopentanoic acid was dose-dependent. The effect of ***coadministration*** of both antagonists was additive in the reduction of sevoflurane minimum alveolar concentration. These results suggest that P2 and NMDA receptors mediate nociceptive/anesthetic processing as inhibition of these receptors resulted in analgesic and anesthetic effects. However the pathway mediated through each receptor may be different postsynaptically and/or one of these presynaptic receptors may modulate the neurotransmitter release of the other.

CONTROLLED TERM: Check Tags: Male; Support, Non-U.S. Gov't
*2-Amino-5-phosphonovalerate: PD, pharmacology
*Anesthetics, Inhalation: PK, pharmacokinetics
Animals
Dose-Response Relationship, Drug
Drug Interactions
*Excitatory Amino Acid Antagonists: PD, pharmacology
Injections, Intraventricular
*Methyl Ethers: PK, pharmacokinetics
Pulmonary Alveoli: DE, drug effects

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Pulmonary Alveoli: ME, metabolism
*Pyridoxal Phosphate: AA, analogs & derivatives
*Pyridoxal Phosphate: PD, pharmacology
Rats
Rats, Sprague-Dawley
*Receptors, N-Methyl-D-Aspartate: AI, antagonists & inhibitors
*Receptors, Purinergic P2: AI, antagonists & inhibitors
Stereoisomerism

REGISTRY NUMBER: **149017-66-3** (pyridoxal phosphate-6-azophenyl-2',4'-disulfonic acid)
28523-86-6 (sevoflurane)
**54-47-7** (Pyridoxal Phosphate)
76726-92-6 (2-Amino-5-phosphonovalerate)

CHEMICAL NAME: 0 (Anesthetics, Inhalation); 0 (Excitatory Amino Acid Antagonists); 0 (Methyl Ethers); 0 (Receptors, N-Methyl-D-Aspartate); 0 (Receptors, Purinergic P2)

L116 ANSWER 19 OF 27 TOXCENTER COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:61874 TOXCENTER
DOCUMENT NUMBER: PubMed ID: 9253943
TITLE: Peripheral adenosine 5'-triphosphate enhances nociception in the formalin test via activation of a purinergic p2X receptor
AUTHOR(S): Sawynok J; Reid A
CORPORATE SOURCE: Department of Pharmacology, Dalhousie University, Halifax, NS, Canada. sawydalu@is.dal.ca
SOURCE: European journal of pharmacology, (1997 Jul 9) 330 (2-3) 115-21.
Journal Code: 1254354. ISSN: 0014-2999.
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDLINE
OTHER SOURCE: MEDLINE 97395956
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20011116

ABSTRACT:
The pronociceptive effects of adenosine 5'-triphosphate (ATP) were examined in the low concentration formalin model (0.5%) by **coadministration** of ATP, ATP analogs (alpha,beta-methylene-ATP and 2-methylthio-ATP) and antagonists (suramin, pyridoxalphosphate-6-azophenyl-2',4'-disulfonic acid) with formalin and determining effects on the expression of flinching behaviours. **Coadministration** of ATP (5-500 nmol) with formalin enhanced phase 2 (12-60 min after injection) but not phase 1 (0-10 min after injection) responses. alpha,beta-methylene-ATP (0.5-50 nmol) but not 2-methylthio-ATP (50-500 nmol) produced a similar enhancement of activity, generating an order of potency of alpha,beta-methylene-ATP, ATP >> 2-methylthio-ATP. This enhancement was primarily expressed in the latter part of phase 2, 30-60 min after injection. **Coadministration** of suramin 50-500 nmol, a non-selective P2X and P2Y purinoceptor antagonist and pyridoxalphosphate-6-azophenyl-2',4'-disulfonic acid 5-500 nmol, a selective P2X purinoceptor antagonist, dose-dependently inhibited the augmentation of the formalin response by ATP 50 nmol, but did not reduce the response to formalin itself. Pretreatment for 30 min with higher doses of suramin inhibited the response to formalin (0.5%, 1.5%) and this appeared to be by a systemically mediated action as it was seen following administration into the contralateral paw. The results of this study provide evidence in support of a P2X purinoceptor mediated augmentation of the pain signal by ATP. The delayed time-course of the effect suggests that it may occur in concert with other mediators that are recruited by the inflammatory process, rather than reflecting a direct depolarization of sensory nerves. Other behavioural

paradigms may be required to examine the fast onset, direct effect. Suramin appears to exert both local and systemic effects on the expression of pain behaviours in response to formalin.

CONTROLLED TERM: Check Tags: Male; Support, Non-U.S. Gov't
Adenosine Triphosphate: AA, analogs & derivatives
*Adenosine Triphosphate: PD, pharmacology
Animals
Behavior, Animal: DE, drug effects
Drug Interactions
*Nociceptors: DE, drug effects
*Nociceptors: PH, physiology
*Pain Measurement: DE, drug effects
Pyridoxal Phosphate: AA, analogs & derivatives
Pyridoxal Phosphate: PD, pharmacology
Rats
Rats, Sprague-Dawley
Receptors, Purinergic P2: CL, classification
*Receptors, Purinergic P2: DE, drug effects
*Receptors, Purinergic P2: PH, physiology
Suramin: PD, pharmacology
Thionucleotides: PD, pharmacology

REGISTRY NUMBER: 145-63-1 (Suramin)
**149017-66-3** (pyridoxal phosphate-6-azophenyl-2',4'-disulfonic acid)
43170-89-4 (2-methylthio-ATP)
**54-47-7** (Pyridoxal Phosphate)
56-65-5 (Adenosine Triphosphate)
7292-42-4 (alpha,beta-methyleneadenosine 5'-triphosphate)

CHEMICAL NAME: 0 (Receptors, Purinergic P2); 0 (Thionucleotides)

L116 ANSWER 20 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-132777 [13] WPIDS
DOC. NO. CPI: C2004-052985
TITLE: Pharmaceutical composition of HMG-CoA reductase inhibitor and pyridoxine for improving blood lipids and reducing blood homocysteine level, for preventing and treating arteriosclerosis, heart disease, cerebral **embolism**, dementia etc..
DERWENT CLASS: B05
INVENTOR(S): KONDO, T; NAKAYAMA, M; TAKAGI, I; TORIZUMI, Y
PATENT ASSIGNEE(S): (SANY) SANKYO CO LTD
COUNTRY COUNT: 105
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 2004006919 | A1 | 20040122 | (200413)* | JA | 33 | A61K031-4415 |

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2004006919 | A1 | WO 2003-JP8674 | 20030708 |

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PRIORITY APPLN. INFO: JP 2002-343586 20021127; JP 2002-202121 20020711

INT. PATENT CLASSIF.:
MAIN: A61K031-4415
SECONDARY: A61K031-22; A61K031-366; A61K031-40; A61K031-675; A61K045-00; A61P003-06; A61P007-02; A61P009-00; A61P009-10; A61P009-10101; A61P025-16; A61P025-28; A61P043-00

BASIC ABSTRACT:

WO2004006919 A UPAB: 20040223

NOVELTY - Pharmaceutical composition comprises a HMG-CoA reductase inhibitor (A) and a pyridoxine (B).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a combination of (A) and (B) (administered separately or together) for improving blood fats or high blood levels of homocysteine.

ACTIVITY - Antilipemic; Antiarteriosclerotic; Cardiant; **Thrombolytic**; Vasotropic; Neuroprotective; Nootropic; Cytostatic; Hepatotropic; Antismoking; Eating Disorders-Gen.;Antidiabetic; Antiparkinsonian; Antithyroid; Antianemic.

Blood levels of total cholesterol, low density lipoprotein (LDL) and triglycerides were measured in beagle dogs. The dogs were given 1 mg/kg simvastatin and/or 50 mg/kg pyridoxine hydrochlorine orally for 11 days, and the blood levels measured on the 12th day. Percentage change, given as (total cholesterol:LDL:triglyceride) was 92.4:81.3:82.0 for simvastatin alone; 90.5:91.4:81.2 for pyridoxine alone; and 80.0:70.4:65.1 for simvastatin and pyridoxine together.

MECHANISM OF ACTION - HMG-CoA reductase inhibitor.

USE - The composition, and (A) and (B) separately, are useful for preventing or treating hyperlipidemia, arteriosclerosis, ischemic heart disease, myocardial infarction, **thrombosis**, disorders of peripheral blood vessels, Burger's disease, Raynaud's disease, cerebral **embolism**, cerebrovascular disorders, senile dementia, Alzheimer's disease or Parkinson's disease (claimed). It is useful in preventing an increase in homocysteine levels associated with age, smoking, nutrition disorders, drug function, reduced kidney function and renal insufficiency, diabetes, insulin resistance, malignant tumors, reduced thyroid function, and pernicious anemia.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B06-D01; B06-D02; B07-A01; B07-D02; B07-D04C; B07-D12; B10-C04A; B14-E11; B14-E12; B14-F01; B14-F01B; B14-F01E; B14-F02; B14-F03; B14-F04; B14-F06; B14-F07; B14-H01; B14-J01A3; B14-J01A4; B14-M01B; B14-M01C; B14-N10; B14-N11; B14-S04

L116 ANSWER 21 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-322621 [30] WPIDS
DOC. NO. CPI: C2004-122980
TITLE: Agent for improving synthetic promotion of e.g. vascular endothelium origin nitrogen oxide concentration, useful for treating e.g. gastrointestinal disorders, includes e.g. soysterol, pyridoxine, riboflavin and/or tocopherols.
DERWENT CLASS: B05
PATENT ASSIGNEE(S): (SANY) SANKYO CO LTD
COUNTRY COUNT: 1
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| JP 2004115507 | A | 20040415 | (200430)* | | 14 | A61K031-16 |

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APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| JP 2004115507 | A | JP 2003-313412 | 20030905 |

PRIORITY APPLN. INFO: JP 2002-260725 20020906
INT. PATENT CLASSIF.:
MAIN: A61K031-16
SECONDARY: A61K031-185; A61K031-355; A61K031-4415; A61K031-455; A61K031-525; A61K031-675; A61P003-00; A61P009-00; A61P013-00; A61P043-00

BASIC ABSTRACT:

JP2004115507 A UPAB: 20040511

NOVELTY - An agent for maintaining and improving synthetic promotion of vascular endothelium origin nitrogen oxide and/or endothelial oxidation azotemia intermediate concentration contains soysterol, pyridoxine, riboflavin, tocopherols, taurine, inositol hexa nicotinate and/or pantethine.

ACTIVITY - Gastrointestinal-Gen.; Respiratory-Gen.; Hypotensive; Antilipemic; Antiarteriosclerotic; Vasotropic; Cardiant; **Thrombolytic**; Antiasthmatic; Hepatotropic; Endocrine-Gen.; Cerebroprotective; Immunomodulator; Antidiabetic.

No test details are given.

MECHANISM OF ACTION - Nitric-Oxide-Synthase-Stimulator.

A 5 months old beagle was administered with the capsule containing nitric oxide synthase promoter. After 11 days 10 ml of blood was taken from cephalic vein and centrifuged to obtain blood serum. The concentration of nitric oxide synthase was evaluated. The result showed that the capsule had significant nitrogen oxide synthase stimulation effect.

USE - The agent is used for the treatment of gastrointestinal disorders, respiratory diseases, hypertension, hyperlipidemia, arteriosclerosis, ischemic heart disease, cardiac failure, **thrombosis**, asthma, COPD, pulmonary hypertension, ARDS, liver cirrhosis, pancreatic inflammation, cerebral ischemia, impotence, immunological disease and diabetes.

ADVANTAGE - The agent is effective in maintaining and improving synthetic promotion of vascular endothelium origin nitrogen oxide and/or endothelial oxidation azotemia intermediate concentration.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B03-C; B03-D; B03-H; B04-J02; B07-D04C; B10-A04; B10-A09B; B14-D01A; B14-E10; B14-F01B; B14-F01E; B14-F02B; B14-F02D; B14-F04; B14-F06; B14-F07; B14-G02D; B14-K01; B14-L01; B14-N07; B14-N12; B14-N13; B14-P02; B14-S04

L116 ANSWER 22 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-332822 [31] WPIDS
DOC. NO. CPI: C2003-086251
TITLE: New heparinoid derivative, useful for treatment, prevention and diagnosis of e.g. degenerative joint disease, comprises chelating group and paramagnetic metal ion.
DERWENT CLASS: B04
INVENTOR(S): JURETSCHKE, H; KERN, C; ULMER, W
PATENT ASSIGNEE(S): (AVET) AVENTIS PHARMA DEUT GMBH; (JURE-I) JURETSCHKE H; (KERN-I) KERN C; (ULME-I) ULMER W

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COUNTRY COUNT: 100
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 2003018640 | A2 | 20030306 | (200331)* | GE | 29 | C08B037-00 |
| RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW | | | | | | |
| W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW | | | | | | |
| DE 10141106 | A1 | 20030313 | (200331) | | | C08B037-10 |
| US 2003109491 | A1 | 20030612 | (200340) | | | C08B037-10 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2003018640 | A2 | WO 2002-EP8909 | 20020809 |
| DE 10141106 | A1 | DE 2001-10141106 | 20010822 |
| US 2003109491 | A1 | US 2002-223145 | 20020819 |

PRIORITY APPLN. INFO: DE 2001-10141106 20010822
INT. PATENT CLASSIF.:
MAIN: C08B037-00; C08B037-10
SECONDARY: A61K031-727; A61K049-12
BASIC ABSTRACT:

WO2003018640 A UPAB: 20030516
NOVELTY - Derivative (A) comprising a heparinoid (I); a chelating agent (II) covalently linked to (I) and a paramagnetic metal cation (III) of scandium, titanium, chromium, vanadium, manganese, iron, cobalt, nickel, copper, molybdenum, ruthenium, lanthanum, cerium, praseodymium, neodymium, promethium, samarium, europium, gadolinium, terbium, dysprosium, holmium, erbium, thulium or ytterbium is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method for preparing (A).

ACTIVITY - Osteopathic; Antiarthritic: Antiinflammatory; Vulnerary; **Antithrombotic**; Cardiant; Vasotropic; Cytostatic; Immunosuppressive; Antiasthmatic.

No biological data is given.

MECHANISM OF ACTION - Aggrecanase, hADAMTS1 (sic) and Gelatinase A Inhibitor.

USE - (A) are used (i) for prevention or treatment of diseases characterized by excessive catabolic activity of proteases, e.g. degenerative joint diseases, osteoarthritis, spondylosis, collagenosis, periodontal diseases, disorders of wound healing, chronic respiratory distress, chronic arthritis, myalgia and disorders of bone metabolism; (ii) for **antithrombotic** prevention or treatment of venous **thrombosis**, aterial thrombotic accidents (e.g. in cardiac infarct, angina, after angioplasty and in treatment of (re)stenosis), treatment of tumors and metastases, inflammation, ischemia, central nervous system disease, transplantation, asthma and angiogenesis; and (iii) for diagnosis, monitoring and functional characterization of diseases where excessive metalloprotease activity is implicated.

ADVANTAGE - (A) can be observed directly at the target site by magnetic resonance imaging, i.e. the local concentration and tissue distribution can be monitored.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN

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MANUAL CODES: CPI: B03-D; B04-B01B; B04-C02; B04-C02E1; B04-E01; B04-N06; B05-A03; B07-D13; B07-E03; B10-B01B; B10-B02J; B12-K04A; B14-C03; B14-C09; B14-F01B; B14-F01D; B14-F01G; B14-F02D; B14-F02F2; B14-F04; B14-G02C; B14-H01; B14-J01; B14-K01A; B14-N01; B14-N06B; B14-N17B

L116 ANSWER 23 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-118013 [12] WPIDS
CROSS REFERENCE: 2004-179097 [17]
DOC. NO. CPI: C2004-047291
TITLE: Reducing platelet aggregation, useful for treating cardiovascular and related disorders, e.g. cerebral ischemia, comprises administering **pyridoxal** or pyridoxine analogs.
DERWENT CLASS: B03
INVENTOR(S): HAQUE, W
PATENT ASSIGNEE(S): (MEDI-N) MEDICURE INT INC
COUNTRY COUNT: 1

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| US 6548519 | B1 | 20030415 | (200412)* | | 27 | C07D401-02 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| US 6548519 | B1 CIP of | US 2001-900718 | 20010706 |
| | | US 2002-147263 | 20020515 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---|---|---|
| US 6548519 | B1 CIP of | US 6417204 |

PRIORITY APPLN. INFO: US 2002-147263 20020515; US 2001-900718 20010706
INT. PATENT CLASSIF.:
MAIN: C07D401-02
SECONDARY: A61K031-44
BASIC ABSTRACT:
US 6548519 B UPAB: 20040310
NOVELTY - Reducing platelet aggregation comprises administering **pyridoxal**/pyridoxine compound (I).

DETAILED DESCRIPTION - Reducing platelet aggregation comprises administering **pyridoxal**/pyridoxine compound of formula (I).

R5 = CH2OH or CHO;

R1 = group of formula (i)-(xii);

n = 1-5;

R2-R4 = H, alkyl, aryl or biaryl (where each aryl or biaryl can be substituted by cyano, alkyl, alkoxy, amino, hydroxy, halo, nitro or alkanoyloxy), amino, acylamino, anilino (where the aniline ring can be substituted by cyano, alkyl, alkoxy, amino, hydroxy, halo, nitro or alkanoyloxy), nitro or guanidino.

ACTIVITY - Anticoagulant; Cardiovascular-Gen.; Hemostatic; Cerebroprotective; Vasotropic; Hypotensive; Cardiant; **Thrombolytic**.

MECHANISM OF ACTION - **Platelet aggregation inhibitor**.

In a test platelet rich plasma was collected by drawing whole blood into sodium citrate tubes and centrifuging at 700 rpm for 10 minutes. Platelet poor plasma was obtained by centrifuging the remainder of the sample until the platelets were removed (3200 rpm for 10 minutes). The plasma collected was used in the test. The extent of aggregation (when test carried out using thrombin receptor activating peptide) for a saline control was 93% compared to only 3% when testing 500 micro M of 4'-((5-Hydroxy-4-hydroxymethyl-6-methyl-pyridin-3-ylmethyl)-amino)-biphenyl-4-carboxamidine (Ia).

USE - For reducing platelet aggregation, (claimed), useful for treating cardiovascular or related diseases, e.g. cerebral ischemia, cerebral hemorrhage, ischemic stroke, hemorrhagic stroke, hypertension, myocardial infarction, ischemia reperfusion injury, myocardial ischemia, congestive heart failure, blood coagulation disorders, cardiac hypertrophy and platelet aggregation, also for treating diseases that arise from thrombotic and prothrombotic states in which the coagulation cascade is activated such as e.g. deep vein **thrombosis**, disseminated intravascular coagulopathy, and pulmonary **embolism**.

Dwg.0/2

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B07-D04C; B14-F01; B14-F02; B14-F04; B14-N16

L116 ANSWER 24 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-179688 [23] WPIDS
DOC. NO. CPI: C2002-055817
TITLE: New pyridoxine and **pyridoxal** analogs for treating cardiovascular or related diseases e.g. cerebral ischemia.
DERWENT CLASS: B03
INVENTOR(S): HAQUE, W
PATENT ASSIGNEE(S): (MEDI-N) MEDICURE INT INC
COUNTRY COUNT: 97
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 2002004421 | A2 | 20020117 | (200223)* | EN | 64 | C07D213-00 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW | | | | | | |
| W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW | | | | | | |
| AU 2001072263 | A | 20020121 | (200234) | | | C07D213-00 |
| US 6417204 | B1 | 20020709 | (200253) | | | C07D401-02 |
| EP 1299358 | A2 | 20030409 | (200325) | EN | | C07D213-40 |
| R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR | | | | | | |
| JP 2004502757 | W | 20040129 | (200413) | | 155 | C07D213-66 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2002004421 | A2 | WO 2001-CA994 | 20010706 |
| AU 2001072263 | A | AU 2001-72263 | 20010706 |
| US 6417204 | B1 Provisional | US 2000-216907P | 20000707 |
| | | US 2001-900718 | 20010706 |
| EP 1299358 | A2 | EP 2001-951279 | 20010706 |
| | | WO 2001-CA994 | 20010706 |
| JP 2004502757 | W | WO 2001-CA994 | 20010706 |

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JP 2002-509088 20010706

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---|---|---|
| AU 2001072263 | A Based on | WO 2002004421 |
| EP 1299358 | A2 Based on | WO 2002004421 |
| JP 2004502757 | W Based on | WO 2002004421 |

PRIORITY APPLN. INFO: US 2000-216907P 20000707; US 2001-900718 20010706

INT. PATENT CLASSIF.:

MAIN: C07D213-00; C07D213-40; C07D213-66; C07D401-02

SECONDARY: A61K031-44; A61K031-4415; A61K031-4427; A61K031-4439; A61K045-00; A61P007-02; A61P009-04; A61P009-06; A61P009-10; A61P009-12; C07D213-48; C07D401-06; C07D401-12

BASIC ABSTRACT:

WO 200204421 A UPAB: 20020411

NOVELTY - Pyridoxine and **pyridoxal** analogs (I) and their acid addition salts are new.

DETAILED DESCRIPTION - Pyridoxine and **pyridoxal** analog compounds of formula (I) and their acid addition salts are new.

R5 = CH2OH or CHO;

R1 = group of formula (i)-(xi) or -(CH2)n-NH-C(=NH)-NH2;

n = 1 - 5;

R2-R4 = H, alkyl or aryl or biaryl (both optionally substituted with T), amino, acylamino, anilino (optionally substituted with T), nitro or guanidino; and

T = cyano, alkyl, alkoxy, amino, hydroxy, halo, nitro or alkanoyloxy.

INDEPENDENT CLAIMS are also included for the following:

(A) treating a cardiovascular or related disease by administering (I) to a mammal in a unit dosage form; and

(B) preparations of (I).

ACTIVITY - Cerebroprotective, Hemostatic; Vasotropic; Hypotensive; Cardiant; Antiarrhythmic; Anticoagulant; **Thrombolytic**; Antibacterial; Immunosuppressive; Antiinflammatory; Antiarteriosclerotic.

Myocardial infarction was produced in male sprague-Dawley rats (300 - 400 g) by occlusion of the left coronary artery. The rats were anaesthetized with isoflurane (1 - 5%) in O2 (100%) (2 l/minute flow rate) and the left anterior descending coronary artery was ligated. Hemodynamic and histological assessments were made. Occlusion of the coronary artery in rats produced myocardial cell damage which resulted in scar formation in the left ventricle and heart dysfunction. While the complete healing of the scar occurred within 3 weeks of the coronary occlusion, mild, moderate and severe stages of congestive heart failure occurred at 4,8 and 16 weeks after ligation. Treatment with **pyridoxal**-5'-phosphate (PLP) and the compound 3-hydroxy-4-hydroxymethyl-2-methyl-5-(4-methylimidazol-1-ylmethyl)pyridine began 1 hour after coronary occlusion and continued for 21 days. Mortality occurred only within the first 24 hours after coronary ligation. While in the untreated group 50% of the rats died, the mortality rate dropped to 17 - 25% in the treated groups.

MECHANISM OF ACTION - None given in the source material.

USE - For treating a cardiovascular or related disease selected from cerebral ischemia, cerebral hemorrhage, ischemic stroke, hemorrhagic stroke, hypertension, myocardial infarction, ischemia reperfusion injury, myocardial ischemia, congestive heart failure, arrhythmia, blood coagulation disorder, cardiac hypertrophy, disease arising from thrombotic and prothrombotic states in which the coagulation cascade is activated e.g. deep vein **thrombosis**, disseminated intravascular

coagulopathy and pulmonary **embolism**; platelet aggregation (all claimed) and peripheral arterial occlusion, for treating adult respiratory distress syndrome, septic shock, septicemia and inflammatory responses e.g. edema and acute or chronic atherosclerosis and for **reducing** or removing blood **clots** in the arteries.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B07-D04; B07-D09; B07-D13; B14-C03; B14-F01A; B14-F01B; B14-F02; B14-F02B; B14-F02B1; B14-F02D; B14-F02D1; B14-F04; B14-F05; B14-F07; B14-F08; B14-J02D1; B14-J02D2; B14-K01F; B14-N08; B14-N16; B14-S06

L116 ANSWER 25 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-607366 [69] WPIDS
DOC. NO. CPI: C2001-180457
TITLE: New pyridoxine phosphonate and malonate derivatives, useful for treating hypertension, myocardial ischemia, cardiovascular diseases, diabetes mellitus and related diseases.
DERWENT CLASS: B02 B03
INVENTOR(S): HAQUE, W
PATENT ASSIGNEE(S): (MEDI-N) MEDICURE INT INC; (HAQU-I) HAQUE W
COUNTRY COUNT: 96
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 2001064692 | A1 | 20010907 | (200169)* | EN | 90 | C07F009-58 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW | | | | | | |
| W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW | | | | | | |
| AU 2001037185 | A | 20010912 | (200204) | | | C07F009-58 |
| US 2002010158 | A1 | 20020124 | (200210) | | | A61K031-675 |
| EP 1268498 | A1 | 20030102 | (200310) | EN | | C07F009-58 |
| R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR | | | | | | |
| US 2003114677 | A1 | 20030619 | (200341) | | | A61K031-675 |
| US 2003114678 | A1 | 20030619 | (200341) | | | C07F009-58 |
| US 2003120074 | A1 | 20030626 | (200343) | | | C07F009-58 |
| US 6605612 | B2 | 20030812 | (200355) | | | A61K031-4415 |
| JP 2003525303 | W | 20030826 | (200357) | | 103 | C07F009-58 |
| US 2003181422 | A1 | 20030925 | (200364) | | | A61K031-675 |
| US 6667315 | B2 | 20031223 | (200408) | | | A61K031-4415 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2001064692 | A1 | WO 2001-CA265 | 20010228 |
| AU 2001037185 | A | AU 2001-37185 | 20010228 |
| US 2002010158 | A1 Provisional | US 2000-185899P | 20000229 |
| | | US 2001-795689 | 20010228 |
| EP 1268498 | A1 | EP 2001-909391 | 20010228 |
| | | WO 2001-CA265 | 20010228 |
| US 2003114677 | A1 Provisional Div ex | US 2000-185899P | 20000229 |
| | | US 2001-795689 | 20010228 |
| | | US 2002-282325 | 20021028 |

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| | | | | |
|---|---|---|---|---|
| US 2003114678 | A1 | Provisional | US 2000-185899P | 20000229 |
| | | Div ex | US 2001-795689 | 20010228 |
| | | | US 2002-282326 | 20021028 |
| US 2003120074 | A1 | Provisional | US 2000-185899P | 20000229 |
| | | Div ex | US 2001-795689 | 20010228 |
| | | | US 2002-282328 | 20021028 |
| US 6605612 | B2 | Provisional | US 2000-185899P | 20000229 |
| | | | US 2001-795689 | 20010228 |
| JP 2003525303 | W | | JP 2001-564188 | 20010228 |
| | | | WO 2001-CA265 | 20010228 |
| US 2003181422 | A1 | Provisional | US 2000-185899P | 20000229 |
| | | Cont of | US 2001-795689 | 20010228 |
| | | | US 2003-377507 | 20030228 |
| US 6667315 | B2 | Provisional | US 2000-185899P | 20000229 |
| | | Div ex | US 2001-795689 | 20010228 |
| | | | US 2002-282326 | 20021028 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO |
|---|---|---|---|
| AU 2001037185 | A | Based on | WO 2001064692 |
| EP 1268498 | A1 | Based on | WO 2001064692 |
| JP 2003525303 | W | Based on | WO 2001064692 |

PRIORITY APPLN. INFO: US 2000-185899P 20000229; US
2001-795689 20010228; US
2002-282325 20021028; US
2002-282326 20021028; US
2002-282328 20021028; US
2003-377507 20030228

INT. PATENT CLASSIF.:
MAIN: A61K031-4415; A61K031-675; C07F009-58
SECONDARY: A61K031-436; A61K031-44; A61K031-662; A61K031-683; A61K038-28; A61K045-00; A61P003-00; A61P003-04; A61P003-10; A61P007-02; A61P009-00; A61P009-04; A61P009-06; A61P009-08; A61P009-10; A61P009-12; A61P013-02; A61P043-00; C07D213-65; C07D213-66; C07D491-056; C07F009-56; C07F009-576; C07F009-6561

BASIC ABSTRACT:
WO 200164692 A UPAB: 20011126
NOVELTY - Pyridoxine phosphonate and malonate derivatives (I) and their salts are new.
DETAILED DESCRIPTION - Pyridoxine phosphonate and malonate derivatives of formula (I) and their salts are new.
X = C(R3)(R4)-P(=O)(OR5)(OR5) (i), CH2-N(R3')-(CH2)n-P(=O)(OR4')(OR4') (ii), C(R3'')(R4'')C(R5'')(R6'')-P(=O)(OR7)(OR7) (iii) or CH(R3''')C(R3a)(CO2R4''')(CO2R4''');
R1 = H or alkyl;
R2 = CHO, CH2OH, Me, -CO2R6, or -CH2-O-alkyl (where alkyl is covalently bonded to O at the 3-position instead of R1);
R6 = H, alkyl or aryl;
R3 = H; and
R4 = OH, halo, alkoxy, alkylcarbonyloxy, alkylamino or arylamino; or
R3 and R4 = halo;
R5 = H, alkyl, aryl, aralkyl or -CO2R7;
R7 = H, alkyl, aryl or aralkyl.
R3', R6' = H, alkyl, aryl or aralkyl;
R4' = R3' or CO2R6';
n = 1-6;
R3'' = H;
R4'' = OH, halo, alkoxy or alkylcarbonyloxy; or

R3''+R4'' = carbonyl;
R5'', R6'' = both halo or both H;
R7 = H, alkyl, aryl, aralkyl or -CO2R8;
R8 = H, alkyl, aryl or aralkyl;
R3''', R3a = H or halo;
R3''' + R3a = a second covalent bond between the C's to which they are attached; and
R4''' = H or alkyl.

ACTIVITY - Hypotensive; cardiant; vasotropic; antiarrhythmic; antidiabetic; anorectic; anticoagulant; **thrombolytic**.

Myocardial infarction was produced in rats by occlusion of the left coronary artery. Rats were treated with (A) **pyridoxal**-5' phosphate, (B) (3-hydroxy-4-hydroxymethyl-2-methyl-5-pyridyl)hydroxymethyl phosphonic acid, or (C) (3-hydroxy-4 hydroxymethyl-2-methyl-5-pyridyl)fluoromethyl phosphonic acid, 10 mg/kg/day by gastric tube. Treatment began 1 hour after coronary occlusion and continued for 21 days. Mortality in all groups occurred only within the first 24 hours after ligation. In an untreated control group 50% of rats died, whereas the mortality rate in the treated groups was 17-25%.

MECHANISM OF ACTION - None given.

USE - For treating hypertension, myocardial infarction, ischemia reperfusion injury, myocardial ischemia, congestive heart failure, arrhythmia, hypertrophy, a disease that arises from thrombotic and prothrombotic states in which the coagulation cascade is activated (e.g. deep vein **thrombosis**, disseminated intravascular coagulopathy, pulmonary **embolism**), diabetes mellitus, insulin resistance, hyperinsulinemia, diabetes-induced hypertension, diabetes-related damage to blood vessels, eyes, kidneys, nerves, autonomic nervous system, skin, connective tissue or immune system; or obesity, and for **reducing** blood **clots** (all claimed).

In the treatment of insulin-dependent diabetes, (I) is administered concurrently with insulin, and in the treatment of non-insulin dependent diabetes or hyperinsulinemia, with insulin or hypoglycemic compound (claimed).

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B04-J03A; B05-B01E; B06-E03; B07-D04B; B07-D04C; B14-E12; B14-F01A; B14-F01B; B14-F02B; B14-F02D; B14-F04; B14-F05; B14-G01; B14-J01; B14-K01; B14-N03; B14-N10; B14-N16; B14-N17; B14-S04

L116 ANSWER 26 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-244268 [25] WPIDS
DOC. NO. CPI: C2001-073256
TITLE: Administration of **pyridoxal**-5'-phosphate and its derivatives in combination with cardiovascular compounds for the treatment of cardiovascular and related diseases.
DERWENT CLASS: B05
INVENTOR(S): HAQUE, W; SETHI, R
PATENT ASSIGNEE(S): (MEDI-N) MEDICURE INC; (MEDI-N) MEDICURE INT INC
COUNTRY COUNT: 95
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 2001013900 | A2 | 20010301 | (200125)* | EN | 84 | A61K031-00 |

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC

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| | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | LK | LR | LS | LT | LU | LV | MA | MD | MG | MK | MN | MW | MX | MZ | NO | NZ | PL | PT | RO | RU | SD | SE |
| | | SG | SI | SK | SL | TJ | TM | TR | TT | TZ | UA | UG | UZ | VN | YU | ZA | ZW | | | | | | |
| AU | 2000068144 | | | | A | 20010319 | (200136) | | | | | | | | | A61K031-00 | | | | | | | |
| EP | 1210117 | | | | A2 | 20020605 | (200238) | | | | | EN | | | | A61K045-06 | | | | | | | |
| | R: | AL | AT | BE | CH | CY | DE | DK | ES | FI | FR | GB | GR | IE | IT | LI | LT | LU | LV | MC | MK | NL | PT |
| | | RO | SE | SI | | | | | | | | | | | | | | | | | | | |
| JP | 2003507418 | | | | W | 20030225 | (200317) | | | | | | | 90 | | A61K031-4355 | | | | | | | |
| US | 6677356 | | | | B1 | 20040113 | (200405) | | | | | | | | | A61K031-445 | | | | | | | |
| US | 2004033989 | | | | A1 | 20040219 | (200414) | | | | | | | | | A61K031-675 | | | | | | | |
| US | 2004033990 | | | | A1 | 20040219 | (200414) | | | | | | | | | A61K031-675 | | | | | | | |
| US | 2004033991 | | | | A1 | 20040219 | (200414) | | | | | | | | | A61K031-675 | | | | | | | |
| US | 2004033992 | | | | A1 | 20040219 | (200414) | | | | | | | | | A61K031-675 | | | | | | | |
| US | 2004033993 | | | | A1 | 20040219 | (200414) | | | | | | | | | A61K031-675 | | | | | | | |
| US | 2004038945 | | | | A1 | 20040226 | (200416) | | | | | | | | | A61K031-675 | | | | | | | |

APPLICATION DETAILS:

| PATENT NO | KIND | | APPLICATION | DATE |
|---|---|---|---|---|
| WO 2001013900 | A2 | | WO 2000-CA1020 | 20000824 |
| AU 2000068144 | A | | AU 2000-68144 | 20000824 |
| EP 1210117 | A2 | | EP 2000-956009 | 20000824 |
| | | | WO 2000-CA1020 | 20000824 |
| JP 2003507418 | W | | WO 2000-CA1020 | 20000824 |
| | | | JP 2001-518038 | 20000824 |
| US 6677356 | B1 | Provisional | US 1999-150415P | 19990824 |
| | | | US 2000-645237 | 20000824 |
| US 2004033989 | A1 | Provisional | US 1999-150415P | 19990824 |
| | | Div ex | US 2000-645237 | 20000824 |
| | | | US 2003-639876 | 20030812 |
| US 2004033990 | A1 | Provisional | US 1999-150415P | 19990824 |
| | | Div ex | US 2000-645237 | 20000824 |
| | | | US 2003-639877 | 20030812 |
| US 2004033991 | A1 | Provisional | US 1999-150415P | 19990824 |
| | | Div ex | US 2000-645237 | 20000824 |
| | | | US 2003-639949 | 20030812 |
| US 2004033992 | A1 | Provisional | US 1999-150415P | 19990824 |
| | | Div ex | US 2000-645237 | 20000824 |
| | | | US 2003-639950 | 20030812 |
| US 2004033993 | A1 | Provisional | US 1999-150415P | 19990824 |
| | | Div ex | US 2000-645237 | 20000824 |
| | | | US 2003-639955 | 20030812 |
| US 2004038945 | A1 | Provisional | US 1999-150415P | 19990824 |
| | | Div ex | US 2000-645237 | 20000824 |
| | | | US 2003-639948 | 20030812 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO |
|---|---|---|---|
| AU 2000068144 | A | Based on | WO 2001013900 |
| EP 1210117 | A2 | Based on | WO 2001013900 |
| JP 2003507418 | W | Based on | WO 2001013900 |

PRIORITY APPLN. INFO: US 1999-150415P 19990824; US
2000-645237 20000824; US
2003-639876 20030812; US
2003-639877 20030812; US
2003-639949 20030812; US
2003-639950 20030812; US
2003-639955 20030812; US
2003-639948 20030812

Searched by Barb O'Bryen, STIC 571-272-2518

INT. PATENT CLASSIF.:
MAIN: A61K031-00; A61K031-4355; A61K031-445; A61K045-06
SECONDARY: A61K031-138; A61K031-165; A61K031-277; A61K031-341; A61K031-401; A61K031-417; A61K031-4415; A61K031-4422; A61K031-4965; A61K031-5377; A61K031-55; A61K031-554; A61K031-616; A61K031-675; A61K031-727; A61K038-55; A61K045-00; A61P007-02; A61P009-00; A61P009-06; A61P009-10; A61P009-12; A61P013-00; A61P043-00; C07D491-048

BASIC ABSTRACT:

WO 200113900 A UPAB: 20010508

NOVELTY - Methods comprising the administration of a composition (I) comprises **pyridoxal**-5'-phosphate, **pyridoxamine**, or 3-acylated **pyridoxal** analogs in combination with cardiovascular compounds.

DETAILED DESCRIPTION - Methods comprising the administration of a composition (I) comprises :

(a) **pyridoxal**-5'-phosphate, **pyridoxal**, **pyridoxamine**, a 3-acylated **pyridoxal** analogue, or their acid salts; and

(b) a cardiovascular compound comprising of an angiotensin converting enzyme inhibitor, an angiotensin II receptor antagonist, a calcium channel blocker, an **antithrombolytic** agent, a ss-adrenergic receptor antagonist, a diuretic, or an I-adrenergic receptor antagonist.

ACTIVITY - Vasotropic; cardiant; antiarrhythmic, anticoagulant; hypotensive.

The concurrent administration of **pyridoxal**-5'-phosphate (P-5-P) and captopril or verapamil on systolic blood pressure (SBP) in 10 % sucrose-induced hypertension in rats was determined. The blood pressure was monitored using the tail cuff method. P-5-P has a significant beneficial effect on SBP in groups where P-5-P treatment is either given alone or in combination with verapamil or captopril, 1 week, the same day and 2 weeks after inducing hypertension in rats with a sucrose source. It has been shown that concurrent administration of P-5-P and captopril or verapamil significantly decreases the sucrose-induced increase in SBP.

MECHANISM OF ACTION - The cardiovascular compound is an angiotensin converting enzyme inhibitor; an angiotensin II receptor antagonists, a calcium channel blocker, a ss-adrenergic receptor antagonist, or an I-adrenergic receptor antagonist.

USE - Compound (I) is used for treating ischemia, congestive heart failure, myocardial infarction, arrhythmia, **reducing** blood **clots**, hypertension, hypertrophy, ischemia reperfusion injury and myocardial ischemia (claimed). The compound may also be administered prior to hear procedures, including bypass surgery, thrombolysis, angioplasty and prior to any other procedures that require blood glow to be interrupted and then resumed.

ADVANTAGE - The combination of administering the compound with a cardiovascular compound, enables the administration of lower dosages than when the cardiovascular compound is administered alone. By administering lower amounts the side effects associated with the active ingredient may be reduced. These side effects include hypotension associated with I-adrenergic receptor antagonist and excessive bleeding associated with **antithrombolytic** agents.

Dwg.0/34

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B04-C02E; B05-B01M; B06-H; B07-H; B14-D03; B14-F01A; B14-F01B; B14-F02B; B14-F02D; B14-F04

L116 ANSWER 27 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-572259 [53] WPIDS
DOC. NO. CPI: C2000-170666

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TITLE: New **pyridoxal** derivatives are useful for the treatment of e.g. vitamin B6 deficiency, interferences in glycolysis, hypertension, myocardial infarction and ischemia reperfusion injury.

DERWENT CLASS: B02 B03

INVENTOR(S): CHARLTON, J L; HAQUE, W

PATENT ASSIGNEE(S): (MEDI-N) MEDICURE INC; (UYMA-N) UNIV MANITOBA; (MEDI-N) MEDICORE INC

COUNTRY COUNT: 91

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 2000053606 | A1 | 20000914 | (200053)* | EN | 50 | C07D491-04 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW | | | | | | |
| W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW | | | | | | |
| AU 2000031834 | A | 20000928 | (200067) | | | |
| US 2001031770 | A1 | 20011018 | (200166) | | | A61K031-4412 |
| EP 1169322 | A1 | 20020109 | (200205) | EN | | C07D491-04 |
| R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MK RO SI | | | | | | |
| US 6339085 | B1 | 20020115 | (200208) | | | A61K031-4375 |
| BR 2000008857 | A | 20011218 | (200209) | | | C07D491-04 |
| JP 2002539127 | W | 20021119 | (200281) | | 62 | C07D213-66 |
| NZ 514567 | A | 20021122 | (200301) | | | C07D491-04 |
| AU 763464 | B | 20030724 | (200355) | | | C07D491-04 |
| US 2003195236 | A1 | 20031016 | (200369) | | | A61K031-4415 |

APPLICATION DETAILS:

| PATENT NO | KIND | | APPLICATION | DATE |
|---|---|---|---|---|
| WO 2000053606 | A1 | | WO 2000-IB255 | 20000307 |
| AU 2000031834 | A | | AU 2000-31834 | 20000307 |
| US 2001031770 | A1 | Provisional | US 1999-123698P | 19990308 |
| | | Provisional | US 1999-125881P | 19990324 |
| | | Div ex | US 2000-520194 | 20000307 |
| | | | US 2001-863093 | 20010522 |
| EP 1169322 | A1 | | EP 2000-909553 | 20000307 |
| | | | WO 2000-IB255 | 20000307 |
| US 6339085 | B1 | Provisional | US 1999-123698P | 19990308 |
| | | Provisional | US 1999-125881P | 19990324 |
| | | | US 2000-520194 | 20000307 |
| BR 2000008857 | A | | BR 2000-8857 | 20000307 |
| | | | WO 2000-IB255 | 20000307 |
| JP 2002539127 | W | | JP 2000-604042 | 20000307 |
| | | | WO 2000-IB255 | 20000307 |
| NZ 514567 | A | | NZ 2000-514567 | 20000307 |
| | | | WO 2000-IB255 | 20000307 |
| AU 763464 | B | | AU 2000-31834 | 20000307 |
| US 2003195236 | A1 | Provisional | US 1999-123698P | 19990308 |
| | | Provisional | US 1999-125881P | 19990324 |
| | | Div ex | US 2000-520194 | 20000307 |
| | | Cont of | US 2001-863093 | 20010522 |
| | | | US 2003-453414 | 20030603 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
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|---|---|---|---|
| AU 2000031834 | A | Based on | WO 2000053606 |
| EP 1169322 | A1 | Based on | WO 2000053606 |
| BR 2000008857 | A | Based on | WO 2000053606 |
| JP 2002539127 | W | Based on | WO 2000053606 |
| NZ 514567 | A | Based on | WO 2000053606 |
| AU 763464 | B | Previous Publ. | AU 2000031834 |
| | | Based on | WO 2000053606 |
| US 2003195236 | A1 | Div ex | US 6339085 |

PRIORITY APPLN. INFO: US 1999-125881P 19990324; US
1999-123698P 19990308; US
2000-520194 20000307; US
2001-863093 20010522; US
2003-453414 20030603

INT. PATENT CLASSIF.:
MAIN: A61K031-4375; A61K031-4412; A61K031-4415; C07D213-66; C07D491-04
SECONDARY: A61K031-44; A61K031-443; A61K031-5377; A61K045-00; A61P003-02; A61P007-00; A61P007-04; A61P009-00; A61P009-04; A61P009-06; A61P009-10; A61P009-12; A61P035-00; A61P043-00; C07D213-62; C07D213-78; C07D413-14; C07D471-02; C07D491-048

BASIC ABSTRACT:

WO 200053606 A UPAB: 20001023

NOVELTY - **Pyridoxal** derivatives (I) and (II) are new.

DETAILED DESCRIPTION - **Pyridoxal** derivatives of formula (I) and (II) and their salts are new.

R1 = alkyl or alkenyl (optionally interrupted by N, O or S and optionally substituted on the terminal C by OH, alkoxy, alkanoyloxy, alkanoyloxyaryl, alkoxyalkanoyl, alkoxycarbonyl or dialkylcarbamoyloxy), alkoxy, dialkylamino, alkanoyloxy, alkanoyloxyaryl, alkoxyalkanoyl, alkoxycarbonyl, dialkylcarbamoyloxy, or aryl, aryloxy, arylthio or aralkyl optionally substituted by alkyl, alkoxy, amino, OH, halogen, nitro or alkanoyloxy; and

R2 = secondary amino.

ACTIVITY - Endocrine; hypotensive; cardiant; vasotropic; antiarrhythmic; anticoagulant; cytostatic; **thrombolytic**.

Blood samples were taken from male Sprague-Dawley rats and after 24-48 hours **pyridoxal**-5'-phosphate (control) or test compounds at 10 mg/kg were administered orally. Blood samples were taken up to 2160 minutes after administration and **pyridoxal**-5'-phosphate and **pyridoxal** levels were determined. (1-Morpholino-1,3-dihydro-7-pivaloyloxy)-6-methylfuro(3,4-c)pyridine (IIa) provided **pyridoxal** and **pyridoxal**-5'-phosphate levels comparable to levels obtained following administration of **pyridoxal**-5'-phosphate.

MECHANISM OF ACTION - None given.

USE - (I) and (II) are useful for the treatment of vitamin B6 deficiency, hyperhomocysteinemia, interferences in glycolysis, aerobic metabolism, biosynthesis of serotonin or biosynthesis of GABA ( gamma -amino butyric acid), hypertension, myocardial infarction, ischemia reperfusion injury, congestive heart failure, arrhythmia, blood coagulation, hypertrophy, deep vein **thrombosis**, disseminated intravascular coagulopathy, pulmonary **embolism** and platelet aggregation (claimed), and melanoma.

ADVANTAGE - (I) have good bioavailability.

Dwg.0/4

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B06-E03; B07-D04; B14-F01A; B14-F01B; B14-F02B; B14-F02B1; B14-F02B2; B14-F02D; B14-F04; B14-F05; B14-H01; B14-J02D1; B14-J02D2; B14-K01; B14-N08

Searched by Barb O'Bryen, STIC 571-272-2518

FILE 'HOME' ENTERED AT 17:10:57 ON 28 MAY 2004

=> fil reg; d ide 119; d ide 120; d ide 121; d stat que 115
FILE 'REGISTRY' ENTERED AT 17:08:06 ON 28 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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STRUCTURE FILE UPDATES: 27 MAY 2004 HIGHEST RN 686710-55-4
DICTIONARY FILE UPDATES: 27 MAY 2004 HIGHEST RN 686710-55-4

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

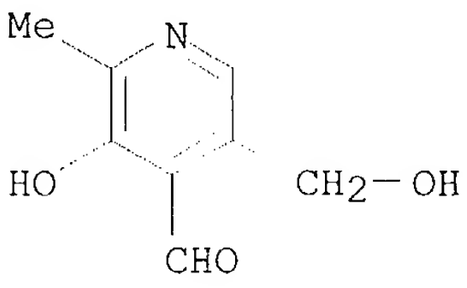
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

L19 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 66-72-8 REGISTRY
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-5-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Pyridoxal (8CI)**
OTHER NAMES:
CN Pyridoxaldehyde
FS 3D CONCORD
MF C8 H9 N O3
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, DDFU, DRUGU, EMBASE, GMELIN*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, RTECS*, SPECINFO, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Searched by Barb O'Bryen, STIC 571-272-2518




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1607 REFERENCES IN FILE CA (1907 TO DATE)
90 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1607 REFERENCES IN FILE CAPLUS (1907 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L20 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 85-87-0 REGISTRY
CN 3-Pyridinemethanol, 4-(aminomethyl)-5-hydroxy-6-methyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Pyridoxamine (8CI)**
OTHER NAMES:
CN 4-(Aminomethyl)-3-hydroxy-5-(hydroxymethyl)-2-methylpyridine
CN Pyridoxylamine
FS 3D CONCORD
MF C8 H12 N2 O2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSRESEARCH, IPA, MEDLINE, SPECINFO, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
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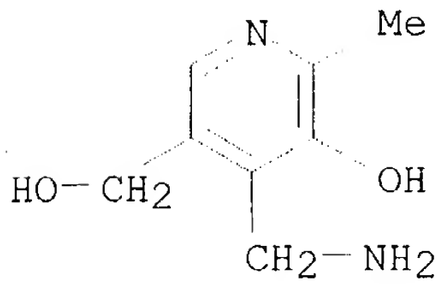
Searched by Barb O'Bryen, STIC 571-272-2518




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

842 REFERENCES IN FILE CA (1907 TO DATE)
41 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
842 REFERENCES IN FILE CAPLUS (1907 TO DATE)
4 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L21 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **54-47-7** REGISTRY
CN 4-Pyridinecarboxaldehyde, 3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]-
(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Pyridoxal phosphate (6CI)
CN Pyridoxal, 5-(dihydrogen phosphate) (8CI)
OTHER NAMES:
CN 2-Methyl-3-hydroxy-4-formyl-5-pyridylmethylphosphoric acid
CN 3-Hydroxy-5-(hydroxymethyl)-2-methylisonicotinaldehyde 5-phosphate
CN Apolon B6
CN Biosechs
CN Codecarboxylase
CN Coenzyme B6
CN Hairoxal
CN Hexermin P
CN Hi-Pyridoxin
CN Hiadelon
CN NSC 82388
CN PAL-P
CN Phosphopyridoxal
CN Phosphopyridoxal coenzyme
CN Piodel
CN PLP
CN Pydoxal
CN Pyridoxal 5'-phosphate
CN Pyridoxal 5-monophosphoric acid ester
CN Pyridoxal 5-phosphate
CN Pyridoxal monophosphate
CN Pyridoxal P
CN Pyridoxaldehyde phosphate
CN Pyridoxyl phosphate
CN Pyromijin
CN Sechvitan
CN Vitahexin P
CN Vitamin B6 phosphate
CN Vitamin B6 phosphate (ester)
CN Vitazechs
FS 3D CONCORD
DR 52064-48-9, 52441-27-7
MF C8 H10 N O6 P
CI COM

Searched by Barb O'Bryen, STIC 571-272-2518

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, GMELIN*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Report

RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)

RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

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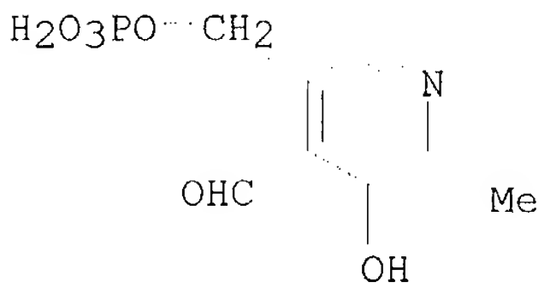
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

5315 REFERENCES IN FILE CA (1907 TO DATE)
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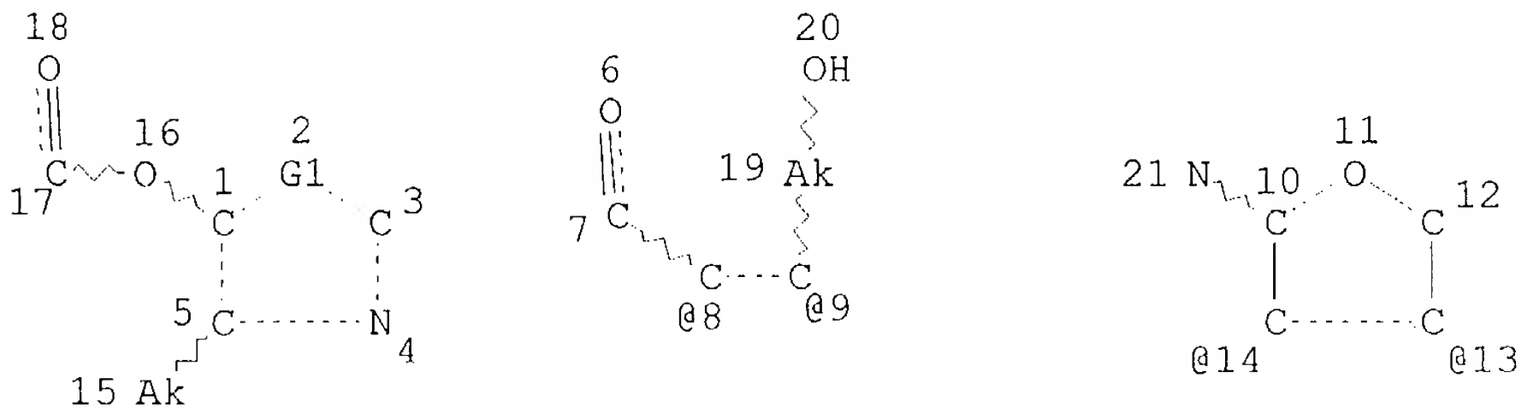
5319 REFERENCES IN FILE CAPLUS (1907 TO DATE)
26 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L13 STR




compounds of claims 2 & 3

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NODE ATTRIBUTES:
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CONNECT IS E1 RC AT 15

Searched by Barb O'Bryen, STIC 571-272-2518

CONNECT IS E2 RC AT 19
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE
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